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	antibodies and agonists or antagonists of	nenhronathy and/or other diseases and disorders as
	the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
	secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
	is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
	insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
	pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
	glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
	proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
•	key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
	assays that may be used or routinely	stroke, and other diseases and disorders as described in the
	modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
	secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
	polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
	antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
	the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
	Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
	2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
	Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
	Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
	(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
	Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
	(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
	herein incorporated by reference in its	highly preferred indications are complications associated
	entirety. Pancreatic cells that may be used	with insulin resistance.
	according to these assays are publicly	
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	pancreatic cells that may be used	
	according to these assays include rat INS-1	
-	cells. INS-1 cells are a semi-adherent cell	
	line established from cells isolated from an	
	X-ray induced rat transplantable	
	insulinoma. These cells retain	
	characteristics typical of native pancreatic	
	beta cells including glucose inducible	
	insulin secretion. References: Asfari et al.	
	Endocrinology 1992 130:167.	

A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders").	Preferred indications include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"), blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Infectious Diseases"). An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is diabeter retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy), sizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart
Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.
Activation of Adipocyte PI3 Kinase Signalling Pathway	
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disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and uninary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	. 5 +
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to
	Activation of Adipocyte ERK Signaling Pathway
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assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
invention (including antibodies and	differentiation. An alternative highly preferred
agonists or antagonists of the invention) to	embodiment of the invention includes a method for
promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	o uo
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the

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				promote or inhibit cell proliferation,	includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include
				assays for ERK kinase activity that may be	neoplastic diseases (e.g., as described below under
				used or routinely modified to test ERK	"Hyperproliferative Disorders"), blood disorders (e.g., as
				kinase-induced activity of polypeptides of	described below under "Immune Activity",
				the invention (including antibodies and	"Cardiovascular Disorders", and/or "Blood-Related
				agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
				include the assays disclosed in Forrer et	, as
				al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
				(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
				64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
				410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
				Prog Biophys Mol Biol 71(3-4):479-500	preferred indications include autoimmune diseases (e.g.,
				(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
				herein incorporated by reference in its	multiple sclerosis and/or as described below) and
				entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
				used according to these assays are publicly	highly preferred indications include inflammation and
				available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
				Exemplary natural killer cells that may be	also include cancers such as, kidney, melanoma, prostate,
				used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
				human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.
				example, NK-YT cells which have	Other preferred indications include benign dysproliferative
				cytolytic and cytotoxic activity) or primary	disorders and pre-neoplastic conditions, such as, for
				NK cells.	example, hyperplasia, metaplasia, and/or dysplasia.
					Other highly preferred indications include, pancytopenia,
					leukopenia, leukemias, Hodgkin's disease, acute
					lymphocytic anemia (ALL), arthritis, asthma, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, psoriasis, immune reactions to transplanted organs
					and tissues, endocarditis, meningitis, Lyme Disease, and
					allergies.
22	HAQAI92	536	Regulation of	Kinase assays, for example an Elk-1 kinase	Preferred embodiments of the invention include using
			proliferation and/or	assay for ERK signal transduction that	polypeptides of the invention (or antibodies, agonists, or
			differentiation in	regulates cell proliferation or	antagonists thereof) in detection, diagnosis, prevention,
			immune cells (such as	differentiation, are well known in the art	and/or treatment of asthma, allergy, hypersensitivity and
			mast cells).	and may be used or routinely modified to	inflammation.
				assess the ability of polypeptides of the	

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includes a method for stimulating MIP Ia production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP Ia production. A highly preferred indication is infection (e.g., an infectious disease as described below under	"Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications	include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meninetits, Lyme Disease, asthma, and	allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as	macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen
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				presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	
24	HATB194	538	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate	as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of	boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 16(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828	malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,

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				(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its	Immune reactions to transplanted organs and ussues,
				entirety. Human dendritic cells that may	nemophilia, nypercoagulation, diabetes mellitus,
_				be used according to these assays may be	3
				isolated using techniques disclosed herein	repertusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
-				and functional activities.	
25	HATCB45	539	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
				modulate the activation of T cells,	suppressing a T cell-mediated immune response.
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
·				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
•				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for

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				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
		-		(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
	4			77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
		4.10		immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
26	HATCD80	540	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the

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	routinely modified to assess the ability of	method for stimulating muscle cell proliferation. In a
	polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is
	antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
	the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
	glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
	Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
	that may be used or routinely modified to	of the invention includes a method for stimulating muscle
	test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
	polypeptides of the invention (including	muscle cell differentiation is stimulated. An alternative
	antibodies and agonists or antagonists of	highly preferred embodiment of the invention includes a
	the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
	Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
	1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
	49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
	Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
	contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
	incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
	Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
	according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
	available (e.g., through the ATCC).	described below under "Immune Activity",
	Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
	used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
	cells. L6 is an adherent rat myoblast cell	., as
	line, isolated from primary cultures of rat	A
	thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
	multinucleated myotubes and striated	additional highly preferred indication is a complication
	fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
		diabetic nephropathy, kidney disease (e.g., renal failure,
		nephropathy and/or other diseases and disorders as
		described in the "Renal Disorders" section below), diabetic
		neuropathy, nerve disease and nerve damage (e.g, due to
		diabetic neuropathy), blood vessel blockage, heart disease,
		stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
-		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,

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	known in the art and may be used or	inactivating B cells. A highly preferred embodiment
	routinely modified to assess the ability of	of the invention includes a method for activating NK cells.
	polypeptides of the invention (including	An alternative highly preferred embodiment of the
	antibodies and agonists or antagonists of	invention includes a method for inhibiting activation of
	the invention) to modulate the activation of	and/or inactivation NK cells. Highly preferred
	T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory
	mediated immunity. Exemplary assays	
	that test for immunomodulatory proteins	Activity"). Preferred indications include blood
	evaluate the upregulation of cell surface	disorders (e.g., as described below under "Immune
	markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
	of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
	or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
-	immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
	polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
	antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
	the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
	assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
	Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
	Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
	approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
	Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
	(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
	(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
	Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
-	460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
	are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
	entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
	according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
	using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
	otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
	are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,
	mature in the thymus and express a T Cell	leukemia, lymphoma, and/or as described below under
	receptor and CD3, CD4, or CD8. These	"Hyperproliferative Disorders"). Preferred indications
	cells mediate humoral or cell-mediated	include neoplasms, such as, for example, leukemia,
	immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
	enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.

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				immunomodulatory factors.	Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
78	натен20	542	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and pre-neoplastic conditions, such as, for example, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include benign dysproliferative disorders and indications include benign dysproliferative disorders and hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, acutropenia, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to

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HBAGD86 543	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994). "Identification of a 30-base pair	transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy) nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders (as described in the "Budocrine disorders (as described in the "Infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tumel syndrome and Dupuytten's contracture). An additional highly preferred indications is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance.
		regulatory element and novel DNA hinding protein that regulates the human	

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.
GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to bind the serum response factor and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in
·	Activation of transcription through serum response element in immune cells (such as T-cells).
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53	HBAGD86	543	Activation of transcription through STAT6 response	Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, mortication, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is asthma. Additional highly preferred indication is asthma. Additional highly preferred indications include inflammation and highly preferred indications preferred indications
			killer cells).	and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the	(e.g., as bod-Rel, ars.). Prars. Prars. Prars. Itiple sciencies ciencies clude neelanoma iferative lasms, s

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4TCC). HBAGD86 543 Activation of transcription transcription through the Gamma Interferon Activation GAS response element are well- in immune cells (such routinely modified to assess the ability of as T-cells). Polypeptides of the invention) to regulate STAT repression involved in a wide variety of transcription factors and may be used or transcription factors and modulate gene element that may be used or routinely modified to test GAS-response element are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation are well- in immune cells (such rough the Gamma Interferon Activation and made are and may be used or routinely represent and may be used or routinely representation and prostate, breast, lung, colon, panceatic, sophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign and/or dysplasia. Preferred indications include autoimmune element that may be used or routinely eryces, rheumatoid arthritis, systemic lupus erychematosis, multiple sclerosis and/or as described element are and may be used or routinely represented in a wide variety of seases (e.g., rheumatoid arthritis, systemic lupus element are activated and prevented in a wide variety of seasons element element are activated and urinary cancer. Other preferred indications include benign and/or as described below under "Hyperplatered in Jumporary Light Programs". Highly preferred in a

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leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infections Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-mediated immune response and alternatively suppressing a
include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Production of IL-6
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				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
		_		the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
		-		proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
		_		modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
•				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
31	HBDAB91	545	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to

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Isulin Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability				is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1995); the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atheroselerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications associated with insulin resistance.
citis. of fourtiles in modified to assess the activity	JAB91	546	1.5	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy,

of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
 is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
 key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
assays that may be used or routinely	stroke, and other diseases and disorders as described in the
modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
 2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
herein incorporated by reference in its	highly preferred indications are complications associated
entirety. Pancreatic cells that may be used	with insulin resistance.
according to these assays are publicly	
available (e.g., through the ATCC) and/or	
may be routinely generated. Exemplary	
pancreatic cells that may be used	
according to these assays include rat INS-1	
cells. INS-1 cells are a semi-adherent cell	
line established from cells isolated from an	
X-ray induced rat transplantable	
insulinoma. These cells retain	
characteristics typical of native pancreatic	
beta cells including glucose inducible	
insulin secretion. References: Asfari et al.	

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				Endocrinology 1992 130:167.	
33	HBGBC29	547	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
			Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth.
			Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
				modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
				polypeptides of the invention (including	growth. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
				the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
				mediated apoptosis. Exemplary assays for	
				caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
				routinely modified to test caspase	preferred embodiment of the invention includes a method
				apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
				invention (including antibodies and	highly preferred embodiment of the invention includes a
				agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
				include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
				al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
				Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
				1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
				Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
				each of which are herein incorporated by	embodiment of the invention includes a method for
				reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
				that may be used according to these assays	embodiment of the invention includes a method for
				are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
				commercial sources). Exemplary	embodiment of the invention includes a method for
				endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
				according to these assays include bovine	preferred embodiment of the invention includes a method
				aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
				an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
				blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
				that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
				angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
				vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
				extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
	-				disease, diabetic nephropathy, intracardiac shunt, cardiac
					hypertrophy, myocardial infarction, chronic hemodynamic
					overload, and/or as described below under
					Cardiovascular Disorders). Highly preferred

12 5 2 4 4 2 5 S	and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculutdes, Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative

disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies hrough (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988):
	Activation of transcription through serum response element in immune cells (such as T-cells).
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			Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and prenepalastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
35 HBHAA05	549	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and	A highly preferred indication is diabetes mellitus. A highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and

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impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain.	highly preferred indications are complications associated with insulin resistance.										A highly preferred indication is diabetes mellitus.	An additional highly preferred indication is a complication	nopathy,	diabetic nephropathy, kidney disease (e.g., renal failure,	orders as	described in the rectal Disorders section below), disorder	ileulopaury, iletve disease and iletve damage (e.g., due to diabetic neutronathy), blood vessel blockage, heart disease.	stroke, impotence (e.g., due to diabetic neuropathy or	onfusion,	drowsiness, nonketotic hyperglycemic-hyperosmolar	isease,	atherosclerosis, microvascular disease, hypertension,	stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,
impaired wound healing, and infection (e.g., infediseases and disorders as described in the "Infection Diseases" section below, especially of the urinary skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred	olications rred indicatiff	complicati										n is diabet	idication i	associated with diabetes (e.g., diabetic retinopathy,	ease (e.g.,	nephropathy and/or other diseases and disorders as	s section	a ve dalita el blockas	iabetic ne	blood vessel blockage), seizures, mental confusion,	cemic-hyp	coma, cardiovascular disease (e.g., heart disease,	sease, hy	sorders as
g, and intas describ as describ w, especia drome an	indication is obesity and/or complication obesity. Additional highly preferred indiweight loss or alternatively, weight gain.	tions are										indicatio	referred in	s (e.g., di	cidney dis	ier disease	i Disoluci	ase allo lie lood vess	, due to di	, seizures	hypergly	lisease (e.	ascular di	ses and di ders" secti
ind healin disorders tion belov tunnel syn	obesity an itional hig r alternati	ed indica										preferred	l highly pı	th diabete	ropathy, l	and/or oth	ile nella	onathy), h	ence (e.g.	blockage)	onketotic	vascular d	is, microv	ther diseas Ilar Disoro
impaired wor diseases and Diseases" sec skin), carpal to contracture).	ication is esity. Add	highly preferred indica with insulin resistance.										A highly	additiona	ociated wi	betic neph	hropathy	CHOCA III	opauly, i betic neur	ke, impot	od vessel	wsiness, n	na, cardio	eroscleros	ske, and or irdiovascu
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nvention) iedrichser (1):136-4 docrinolo R, et al., J	3):17771-9 which is ce in its	may be us ublicly	'CC) and/ xemplary	ed ide rat IN	dherent co	ated from	<u>e</u>	300	e pancreau ducible	Asfari et		n of insuli	nay be us	the abilit	n (includi	igonists of		n secretion nti-rat	retion from	lated by		lation is a	xemplary	tinely 1 of insuli
ts of the ised in: Fr crinol, 15 et al., En); Hugl S	10;273(28 of each of veferen	cells that says are p	gh the AT erated. E	may be us savs inclu	e a semi-a	cells isol	nsplantab	ells retain	d of native	ferences:	130:167	gsecretion	e art and 1	to assess	e inventic	sts or anta	idiate ilist	Dic, Ilisuii Tusine a	nsulin sec	is upregu	ertain	d disregu	abetes. E	sed or rou timulation
antagonis ays disclo Mol Endo otari MA, 4-9 (1998	1998 Jul contents	ancreatic o these as	e.g., throutinely gen	cells that of these as	1 cells are	shed from	ced rat tra	. These c	nes typica neluding s	etion. Re	ogy 1992	measuring	own in th	/ modified	ides of th	and agoni	ony to sum	roi exallij i bv FMA	bodies. In	beta cells	dalso by	ptides, an	nent in di	may be u: test for s
agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J	Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its	entirety. Parcreatic cells that may be used according to these assays are publicly	available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	pancreatic cells that may be used according to these assavs include rat INS-1	cells. INS-1 cells are a semi-adherent cell	line established from cells isolated from an	X-ray induced rat transplantable	insulinoma. These cells retain	cnaracteristics typical of native pancreatic beta cells including olucose inducible	insulin secretion. References: Asfari et al.	Endocrinology 1992 130:167	Assays for measuring secretion of insulin	are well-known in the art and may be used	or routinely modified to assess the ability	of polypeptides of the invention (including	antibodies and agonists or antagonists of	ure invention) to sumulate insumi	sectedum. For example, insum sectedum is measured by FMAT using anti-rat	insulin antibodies. Insulin secretion from	pancreatic beta cells is upregulated by	glucose and also by certain	proteins/peptides, and disregulation is a	key component in diabetes. Exemplary	assays that may be used or routinely modified to test for stimulation of insulin
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				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
				Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
				of each of which is herein incorporated by	with insulin resistance.
				reference in its entirety. Pancreatic cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC) and/or may be routinely generated.	
				Exemplary pancreatic cells that may be	
				used according to these assays include	
				HITT15 Cells. HITT15 are an adherent	
				epithelial cell line established from Syrian	
				hamster islet cells transformed with SV40.	
			*	These cells express glucagon,	
				somatostatin, and glucocorticoid receptors.	
				The cells secrete insulin, which is	
				stimulated by glucose and glucagon and	
				suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
36	HBHAA81	550		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune

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	macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
-	MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
	immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
	T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
	of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
	helper cell functions are well known in the	Highly preferred indications include autoimmune disease
	art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
	invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
	agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
	mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
	inflammatory activities, modulate TH2	indications include inflammation and inflammatory
	helper cell function, and/or mediate	disorders. Additional preferred indications include
	humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
	Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
	immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
	production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
	gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
	cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
	routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
-	immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
	polypeptides of the invention (including	include benign dysproliferative disorders and pre-
	antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
	the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
	in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
	Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
	Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
	J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
	Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
	(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
	15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
	Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
	of each of which are herein incorporated	
	by reference in its entirety. Human T cells	
	that may be used according to these assays	
	may be isolated using techniques disclosed	

				herein or otherwise known in the art	
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
37	HBIAA59	551	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			•	or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	o uo
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
•				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
			-	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An

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that may be used according to these assays	additional highly preferred indication is a complication
adherent mouse preadipocyte cell line that	associated with diabetes (e.g., diabetic retinopatify, diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	hies,
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and
	breast, colon, and kidney cancer. Additional preferred
	indications include melanoma, prostate, lung, pancreatic,
	esophageal, stomach, brain, liver, and urinary cancer.

					Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
38	HBIAC29	552	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL.), piasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous

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					nisease, initialimatory bower disease, incuriopenia, neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
+	DICTOR	553	D. d f	TEN INT TANKE	Mindel Illiectious Disease).
н 	HBICW31	555		IFNgamma FMAI. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
				invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
				agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
				mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
				inflammatory activities, modulate TH2	indications include inflammation and inflammatory
				helper cell function, and/or mediate	disorders. Additional preferred indications include
				humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
				Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
				immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
				production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
				gamma (FNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
				immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
				polypeptides of the invention (including	include benign dysproliferative disorders and pre-
				antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,

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e assays disclosed metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, pancytopenia, leukopenia, thrombocytopenia, pancytopenia, et include anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. Human T cells ing to these assays chniques disclosed wn in the art. ary human is in the thymus and craw and craw and craw and craw and may be responsiveness to ors.	lcium flux are demodiments of the invention include using de may be used or sess the ability of antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Bone and Cartilage Diseases, including or antagonists of but not limited to Arthritis, Cartilige repair, Bone Repair, osteoporosis, and related tumors including chondrosarcomas, chondroblastomas, and chondromas. ared to much ium. Extracellular ux of calcium, calcium, calcium responsive alterations in cell says that may be ed to measure cytes include
the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in chondrocytes include
	Calcium flux in chondrocytes
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assays disclosed in: Asada S, et al., Inflamm Res, 50(1):19-23 (2001); Schwartz Z, et al., J Bone Miner Res, 6(7):709-718 (1991); Iannotti JP, et al., J Bone Joint Surg Am, 67(1): 113-120 (1985); Sullivan E., et al., Methods Mol Biol 1999; 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include bovine chondrocytes.	expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of remnine diseases. Overexpression of remnine autoimmune diseases. Overexpression of remnine diseases. Overexpression of remnine diseases. Overexpression of remnine diseases. Overexpression of real immunoresponses. Assays for immunoresponses. Assays for immunoresponses. Assays for immunoresponses. Assays for immunoresponses and the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD152 may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies of the invention) to modulate the activation of T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for simulating T cell proliferation. Highly preferred indications include autoimmune diseases (e.g., as described agonists or antagonists of the invention) to modulate the activation of cell-mediated maintain T cell homeostasis, and/or mediate humoral or cell-mediated immuniny. Exemplary assays that test for immunomodulatory proteins evaluate the care with the coll surface markers, such as, for example, levening and the proliferative provening includes a method for stimulation of cell surface markers, such as, for example, includes a method for inhibiting T cell mediated by preferred indications of the invention includes a method for inhibiting T cell proprieting antibode and the invention includes a method for simulating the activating of T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proprieting antibode and the invention includes a method for inhibiting T cell proprieting antibode and the invention includes a method for simmune of the invention includes a method for inhibiting T cell proliferation of ce
	Upregulation of T cells and activation of T cells
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				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
_				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
41	HBJAC65	555	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,

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				cell functions. Exemplary assays for transcription through the GAS response	such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune
				element that may be used or routinely modified to test GAS-response element	diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
					immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus,
			- i i		endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
45	HBJBM12	556	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
			-	and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly

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				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
		·····.		cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
43	HBJCR46	557	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.

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pancreatic beta cells.	Known in the art and may be used of	associated with that tells, that the same of the same
	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
	antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
	the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
	proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
	example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
	cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
	viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
	quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
	signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
	active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
	used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
	regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
	pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
	invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
	agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
	include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
	BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
	(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
	139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
	Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
	(1998), the contents of each of which is	obesity. Additional highly preferred indications include
	herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
	entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
	according to these assays are publicly	with insulin resistance.
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
-	pancreatic cells that may be used	
	according to these assays include rat INS-1	
	cells. INS-1 cells are a semi-adherent cell	
	line established from cells isolated from an	
	X-ray induced rat transplantable	
	insulinoma. These cells retain	
	characteristics typical of native pancreatic	
	beta cells including glucose inducible	

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				insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
4	HBJDS79	558	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative
			allu acuvauoli oi 1 celis	CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
· •				proliferation. Reduced CD152 expression	ot.
	·			has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired imminoresponses. Assays for	proliteration. An atternative highly preferred embodiment of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
				modulate the activation of T cells,	suppressing a T cell-mediated immune response.
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin minimulo 11(3).234-300 (1333), and	hypercuaguiation, diadetes inclinus, chuocalums,

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Saito T, Curr Opin Immunol 10(3):313- are herein incorporated by reference in its entirety. Human T cells that may be used using techniques disclosed herein or otherwise known in the art. Human T cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication fecals in vitro are well-associated with diabetes (e.g., diabetic retinopathy, routinely modified to assess the ability of diabetic nephropathy and/or other diseases and disorders as antibodies and agonists or antagonists of the invention of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of without and proficeration of pancreatic beta cells in culture based on cell viability assay measures the number of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of metabolically and processing of the invention (including antibodies and agonists or antagonists of the invention) had a al., Edictions and agonists or antagonists or antagonism of the antianty
Sa are en ac en cot en are en are en are en are en are en im en im	Regulation of viability As and proliferation of propancreatic beta cells. To po an an the proliferation of propancreatic beta cells. To propancreatic beta cells. The propancreatic beta cells and acceptable and accept
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1-9 indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. INS-1 I cell om an eatic et al.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen
	Regulation of viability and proliferation of pancreatic beta cells.
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Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for activation B cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating B cells. A highly preferred embodiment of the invention includes a method for activating NK cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting activation of and/or inactivation NK cells. Highly preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity"). Preferred indications include blood disorders (e.g., as described below under "Immune
BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface
	Upregulation of T cells and activation of T cells
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	HBJEL16
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				markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
				of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
				or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
				polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
				antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
				approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
				(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
				Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
_				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
				are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
				entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
				according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
				using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
				otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
				are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,
				mature in the thymus and express a T Cell	leukemia, lymphoma, and/or as described below under
				receptor and CD3, CD4, or CD8. These	"Hyperproliferative Disorders"). Preferred indications
				cells mediate humoral or cell-mediated	include neoplasms, such as, for example, leukemia,
				immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
				enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
				immunomodulatory factors.	Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
					example, hyperplasia, metaplasia, and/or dysplasia.
47	HBJFK45	561	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkiu s lymphoma, non-riougkins lymphoma, riougkins

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				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				6:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
					immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
47	HBJFK45	561	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			cells (such as natural	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			killer cells).	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),

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iditional infectious sease"). (e.g., under titions pple, colon, lurinary memia, ddor nemia, acytomas, AIDS, ase, ression of ues, and	on vival An vvention vival. es a In a ration is
ne response, ar mune response, ar mune response ations include lisorders. An a ection (e.g., an "Infectious Diplastic diseases (escribed below Preferred indicuch as, for examens include bening brain, liver an ns include bening a also include a salso include a socytopenia, Haia (ALL), plasminghoma, arthritistory bowel dissipportasis, supplement in organs and tissabetes mellitus bisease, asthma bi	nt of the invent muscle cell sur odiment of the i muscle cell su nvention inclue stll proliferation
mediated immu- mediated immu- ell-mediated im inflammatory of inflamma, and/or as of inflamma, and prostat ageal, stomach, ferred indication ple, hyperplasit erred indication kopenia, throm inhocytic anem a, Burkitt's lym sease, inflamma ia, neutrophilia, is to transplantec reoagulation, di ingitis, Lyme I ingitis, Lyme I	A highly preferred embodiment of the invention ludes a method for increasing muscle cell survivariative highly preferred embodiment of the inveludes a method for decreasing muscle cell survivareferred embodiment of the invention includes thought for stimulating muscle cell proliferation. In cific embodiment, skeletal muscle cell proliferat
boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is
regulate NFA1 tors and modul. nes involved in ory functions. ription through it that may be u ed to test NFA7 of polypeptides ling antibodies gonists of the in isclosed in Berj 998); Cullen at ymol 216:362-3 Proc Natl Acad (1998); Arambun 1:801-810 (1997); Fras 3801-810 (1999); Fras 3810 Chem 268 in incorporated by incorporated by the contents of e incorporated by the contents of the con	inase assays, for assay, for PI? on that regulate cell survivial a and may be use ed to assess the invention (i
the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998), Cullen and Malm, Methods in Enzymol 216:362-368 (1992), Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway
	Activation of Skeletal Mucle Cell P13 Kinas Signalling Pathway
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	HBJIG20
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	antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
	the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
	glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
	Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
	that may be used or routinely modified to	of the invention includes a method for stimulating muscle
	test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
	polypeptides of the invention (including	muscle cell differentiation is stimulated. An alternative
	antibodies and agonists or antagonists of	highly preferred embodiment of the invention includes a
	the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
	Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
	1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
	49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
	Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
	contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
	incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
	Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
-	according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
	available (e.g., through the ATCC).	described below under "Immune Activity",
	Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
	used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
	cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
	line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
	thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
	multinucleated myotubes and striated	additional highly preferred indication is a complication
	fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
		diabetic nephropathy, kidney disease (e.g., renal failure,
		nephropathy and/or other diseases and disorders as
		described in the "Renal Disorders" section below), diabetic
		neuropathy, nerve disease and nerve damage (e.g, due to
		diabetic neuropathy), blood vessel blockage, heart disease,
		stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,

		_			
					endocrine disorders (as described in the Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infections (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below, especially of the urinary tract and
					skin), carpal tunnel syndrome and Dupuytren's
					contracture). An additional highly preferred indication
					is obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					preferred indications are complications associated with
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal system
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include: myopathy, atrophy, congestive heart
					failure, cachexia, myxomas, fibromas, congenital
					cardiovascular abnormalities, heart disease, cardiac arrest,
					heart valve disease, and vascular disease. Highly
					preferred indications include neoplasms and cancer, such
					as, rhabdomyoma, rhabdosarcoma, stomach, esophageal,
					prostate, and urinary cancer. Preferred indications also
					include breast, lung, colon, pancreatic, brain, and liver
					cancer. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, hyperplasia, metaplasia, and/or dysplasia.
49	HBJKD16	563	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as

mediated immune response and alternatively suppressing a Other preferred indications include benign dysproliferative neutrophilia, psoriasis, suppression of immune reactions to Highly preferred indications include preferred indications include neoplasms and cancers, such An additional preferred disorders. Additional highly preferred indications include lymphocytic anemia (ALL), multiple myeloma, Burkitt's leukopenia, thrombocytopenia, Hodgkin's disease, acute preferred indications include autoimmune diseases (e.g., melanoma, and prostate, breast, lung, colon, pancreatic, immunodeficiencies (e.g., as described below). Highly B cell-mediated immune response. Highly preferred leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly esophageal, stomach, brain, liver and urinary cancer. described below under "Infectious Disease"). Highly disorders and pre-neoplastic conditions, such as, for preferred indications also include boosting a B cell-Preferred indications include anemia, pancytopenia, indication is infection (e.g., an infectious disease as indications include inflammation and inflammatory example, hyperplasia, metaplasia, and/or dysplasia. as, myeloma, plasmacytoma, leukemia, lymphoma, lymphoma, arthritis, AIDS, granulomatous disease, neoplastic diseases (e.g., myeloma, plasmacytoma, rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and hypercoagulation, diabetes mellitus, endocarditis, inflammatory bowel disease, sepsis, neutropenia, described below under "Infectious Disease"). transplanted organs and tissues, hemophilia, meningitis, and Lyme Disease. asthma and allergy. of polypeptides of the invention (including disclosed herein or otherwise known in the immunomodulation and differentiation and differentiation factor proteins produced by modulate T cell proliferation and function. 204(1999); Rowland et al., "Lymphocytes: diffferentiation activity of polypeptides of are well known in the art and may be used production of cytokines, such as IL-6, and include assays disclosed in Miraglia et al., or routinely modified to assess the ability Such assays that may be used or routinely reference in its entirety. Human dendritic immunomodulatory proteins evaluate the the stimulation and upregulation of T cell antibodies and agonists or antagonists of each of which are herein incorporated by cells that may be used according to these cytokines, growth factors, and hormones a practical approach" Chapter 6:138-160 expression level is strongly regulated by which, when activated by antigen and/or modified to test immunomodulatory and agonists or antagonists of the invention) (2000); and Verhasselt et al., J Immunol assays may be isolated using techniques the invention (including antibodies and cytokines, initiate and upregulate T cell 158:2919-2925 (1997), the contents of art. Human dendritic cells are antigen proliferation and functional activities. presenting cells in suspension culture, proliferation and functional activities. J Biomolecular Screening 4:193a large variety of cells where the Exemplary assays that test for the invention) to mediate

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A highly preferred embodiment of the invention includes a method for stimulating MIP Ia production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP Ia production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g. leukemia, lymphoma, and/or as described	below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
MIP-Ialpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell	differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the
Production of MIP1alpha		
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HBJKD16		
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				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
	=			cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
49	HBJKD16	563	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
		_		the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	nune
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	

				according to these assays include HITT15 Cells. HITT15 are an adherent epithelial	
				cell line established from Syrian hamster	
				islet cells transformed with SV40. These	
				cells express glucagon, somatostatin, and	
				glucocorticoid receptors. The cells secrete	
				insulin, which is stimulated by glucose and	
				glucagon and suppressed by somatostatin	
				or glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
20	HBMBM96	564	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
			_	activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
			_	Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred

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			the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
51 HBMBX01	265	Upregulation of T cells and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., theumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,

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				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
52	HBMTM11	999	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
			Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth.
			Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
				modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
				polypeptides of the invention (including	growth. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
				the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
				mediated apoptosis. Exemplary assays for	шe
				caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
				routinely modified to test caspase	preferred embodiment of the invention includes a method

apoptosis rescue of polypeptides of the invention (including antibodies and	for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a
agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. highly preferred embodiment of the invention includes a
al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
each of which are herein incorporated by	embodiment of the invention includes a method for
reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
that may be used according to these assays	embodiment of the invention includes a method for
are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
 commercial sources). Exemplary	embodiment of the invention includes a method for
endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
according to these assays include bovine	preferred embodiment of the invention includes a method
aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
 that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
	disease, diabetic nephropathy, intracardiac shunt, cardiac
	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred
	indications include cardiovascular, endothelial and/or
	angiogenic disorders (e.g., systemic disorders that affect
	vessels such as diabetes mellitus, as well as diseases of the
	vessels themselves, such as of the arteries, capillaries,
	veins and/or lymphatics). Highly preferred are indications
	that stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms

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and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary	cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	angioplasty, and atheroschlerotic lesions), implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly	preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative	disorders, vascularitis, lymph angiogenesis, sexual	disorders, age-related macular degeneration, and treatment	/prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,	heart disease, cardiac arrest, heart valve disease, and	vascular disease. Preferred indications include blood	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described

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below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease, and pain management.	Production of IL-6 IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases 24 production (Ig.A plays a role in mucosal immunity). IL-6 induces a method for stimulating (e.g., increasing) IL-6 participates in IL-4 induced IgE production the invention includes a method for stimulating (e.g., increasing) IL-6 participates in IL-4 induced IgE production of the invention includes a method for inhibiting (e.g., production of content index of a undimmunity). IL-6 induces cytosoxic T cells. Dergulated expression for IL-6 has been inked to audinimum the disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and disease, plasmacytomas, myelomas, and peruson level is strongly tregulated by expression level is strongly tregulated by expression level is strongly tregulated by crountinely modified to assess the ability of proferred indications along include boosing a Beerral indications include inflammatory immunomodulation and differentiation and mediated Immunomodulatory and discussions of the invention (including and indications include inflammatory and indications include inflammatory immunomodulatory and discussions of the invention of the invention of the prophesited seases the ability. Exemplary assays that test for any proteins evaluate the production of cytokines, such as IL-6, and peruson and indications include inflammatory and inflammatory and inflammatory and indications include inflammatory and indications include inflammatory and indications include inflammatory and indications include inflammatory and evel modulatory and progulation of T cell invention of the preferred indications include the proplement. Such as any progression of the invention o

				204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., I Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell	lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
1	HBMTY48	568	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for P13 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):265-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred indications include disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"), endocrine Disorders", neural

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	Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
	according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
	available (e.g., through the ATCC).	described below under "Immune Activity",
	Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
	used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
	cells. L6 is an adherent rat myoblast cell	, as
	line, isolated from primary cultures of rat	A
	thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
	multinucleated myotubes and striated	additional highly preferred indication is a complication
	fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
		diabetic nephropathy, kidney disease (e.g., renal failure,
		nephropathy and/or other diseases and disorders as
		described in the "Renal Disorders" section below), diabetic
		neuropathy, nerve disease and nerve damage (e.g, due to
		diabetic neuropathy), blood vessel blockage, heart disease,
		stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
-		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infections (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below, especially of the urinary tract and
		skin), carpal tunnel syndrome and Dupuytren's
		contracture). An additional highly preferred indication
		is obesity and/or complications associated with obesity.
		ndicatic
		or alternatively, weight gain. Additional highly
		preferred indications are complications associated with
		insulin resistance. Additonal highly preferred
		indications are disorders of the musculoskeletal system
		including myopathies, muscular dystrophy, and/or as

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•				described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as hymeralasia metaplasia and/or dysplasia
55 HBMUH74	269	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesis. Malic enzyme is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in adipocoytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic retinopathy, diabetes as described in the "Renal Disorders" section below), diabetic neuropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious diseases and disorders as described in the "Infectious bliseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred mith indication is obesity and/or complications associated with

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			1., ct al., J Diol Chem, 274(2).11997-5004 (1999); Ijpenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the H4IIE rat liver	weight loss of anctuatively, weight gain. highly preferred indications are complications associated with insulin resistance.
56 HBMWE61	270	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity," "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described

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				production of cytokines. such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
•				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
a .				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
57 H	HBNAX40	571	Activation of	Assays for the activation of transcription	A highly preferred indication includes allergy. A
			transcription through	through the GATA3 response element are	highly preferred indication includes asthma. A highly
			GATA-3 response	well-known in the art and may be used or	preferred indication includes rhinitis. Additional highly
			element in immune	routinely modified to assess the ability of	preferred indications include infection (e.g., an infectious
			cells (such as T-cells).	polypeptides of the invention (including	disease as described below under "Infectious Disease"),
				antibodies and agonists or antagonists of	and inflammation and inflammatory disorders.
				the invention) to regulate GATA3	Preferred indications include blood disorders (e.g., as
•				transcription factors and modulate	described below under "Immune Activity", "Blood-
				expression of genes important for Th2	Related Disorders", and/or "Cardiovascular Disorders").
				immune response development.	Preferred indications include autoimmune diseases (e.g.,
				Exemplary assays for transcription through	rheumatoid arthritis, systemic lupus erythematosis,
				the GATA3 response element that may be	multiple sclerosis and/or as described below) and
				used or routinely modified to test GATA3-	immunodeficiencies (e.g., as described below).

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	:			response element activity of polypeptides	Preferred indications include neoplastic diseases (e.g.,
				of the invention (including antibodies and	leukemia, lymphoma, melanoma, and/or as described
				agonists or antagonists of the invention)	below under "Hyperproliferative Disorders"). Preferred
				include assays disclosed in Berger et al.,	indications include neoplasms and cancer, such as, for
				Gene 66:1-10 (1998); Cullen and Malm,	example, leukemia, lymphoma, melanoma, and prostate,
				Methods in Enzymol 216:362-368 (1992);	breast, lung, colon, pancreatic, esophageal, stomach,
				Henthorn et al., Proc Natl Acad Sci USA	brain, liver and urinary cancer. Other preferred indications
				85:6342-6346 (1988); Flavell et al., Cold	include benign dysproliferative disorders and pre-
				Spring Harb Symp Quant Biol 64:563-571	neoplastic conditions, such as, for example, hyperplasia,
				(1999); Rodriguez-Palmero et al., Eur J	metaplasia, and/or dysplasia. Preferred indications
				Immunol 29(12):3914-3924 (1999); Zheng	include anemia, pancytopenia, leukopenia,
				and Flavell, Cell 89(4):587-596 (1997);	thrombocytopenia, leukemias, Hodgkin's disease, acute
				and Henderson et al., Mol Cell Biol	lymphocytic anemia (ALL), plasmacytomas, multiple
				14(6):4286-4294 (1994), the contents of	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				each of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. T cells that may	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				be used according to these assays are	immune reactions to transplanted organs and tissues,
				publicly available (e.g., through the	hemophilia, hypercoagulation, diabetes mellitus,
				ATCC). Exemplary mouse T cells that	endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays	
				include the HT2 cell line, which is a	
				suspension culture of IL-2 dependent T	
				cells that also respond to IL-4.	
28	HBNBJ76	572	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described

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				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
58	HBNBJ76	572	Production of RANTES	RANTES FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that induce	includes a method for stimulating RANTES production.
				chemotaxis of T cells, monocytes, and	An alternative highly preferred embodiment of the
				eosinophils are well known in the art and	invention includes a method for inhibiting (e.g., reducing)
				may be used or routinely modified to	RANTES production. A highly preferred indication is
				assess the ability of polypeptides of the	infection (e.g., an infectious disease as described below
				invention (including antibodies and	under "Infectious Disease"). A most highly preferred
				agonists or antagonists of the invention) to	indication includes AIDS and/or the prevention or
				mediate immunomodulation, induce	reduction of HIV infection. Additional highly preferred
				chemotaxis, and/or mediate humoral or	indication includes immune disorders, for example,
				cell-mediated immunity. Exemplary	inflammation and inflammatory disorders. Preferred
				assays that test for immunomodulatory	indications include blood disorders (e.g., as described
				proteins evaluate the production of	below under "Immune Activity", "Blood-Related
				cytokines, such as RANTES, and the	Disorders", and/or "Cardiovascular Disorders"). Highly
				induction of chemotactic responses in	preferred indications include autoimmune diseases (e.g.,

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				immune cells. Such assays that may be	rheumatoid arthritis, systemic lupus erythematosis,
				used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications also include anemia, pancytopenia,
				antibodies and agonists or antagonists of	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				the invention) include the assays disclosed	lymphocytic anemia (ALL), plasmacytomas, multiple
				in Miraglia et al., J Biomolecular	myeloma, Burkitt's lymphoma, arthritis, asthma,
				Screening 4:193-204 (1999); Rowland et	granulomatous disease, inflammatory bowel disease,
				al., "Lymphocytes: a practical approach"	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				Chapter 6:138-160 (2000): Cocchi et al.,	immune reactions to transplanted organs and tissues,
				Science 270(5243):1811-1815 (1995); and	hemophilia, hypercoagulation, diabetes mellitus,
				Robinson et al., Clin Exp Immunol	endocarditis, meningitis, Lyme Disease, asthma, and
				101(3):398-407 (1995), the contents of	allergy. Highly preferred indications also include
				each of which are herein incorporated by	neoplastic diseases (e.g., leukemia, lymphoma, and/or as
				reference in its entirety. Human immune	described below under "Hyperproliferative Disorders").
				cells that may be used according to these	Highly preferred indications include neoplasms, such as,
				assays may be isolated using techniques	for example, leukemia, lymphoma, prostate, breast, lung,
				disclosed herein or otherwise known in the	colon, pancreatic, esophageal, stomach, brain, liver, and
				art.	urinary cancer. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia.
59	HBQAB79	573	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	Cardiovascular Disorders section below), dyslipidemia,

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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include neoplastic diseases (e.g., as described below under
secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992, 130:167.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	Activation of Natural Killer Cell ERK Signaling Pathway.
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ne invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells. Activation of Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may in immune cells (such be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate

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				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
62	HBXCM66	576	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response in	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			immune cells (such as	known in the art and may be used or	Disorders"). Highly preferred indications include
			T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			-	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described

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			antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
			may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	
63 HBXCX15	577	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic

the invention) to activate the DMEF1	neuropathy nerve disease and nerve damage (e.g., due to
response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
(such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
another transcription factor that is required	stroke, and other diseases and disorders as described in the
for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
 test for DMEF1 response element activity	diseases and disorders as described in the "Infectious
(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
polypeptides of the invention (including	skin), carpal tunnel syndrome and Dupuytren's
antibodies and agonists or antagonists of	contracture). An additional highly preferred
the invention) include assays disclosed	indication is obesity and/or complications associated with
inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
 J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
21 (1994); "Identification of a 30-base pair	
regulatory element and novel DNA	
binding protein that regulates the human	
GLUT4 promoter in transgenic mice", J	
Biol Chem. 2000 Aug 4;275(31):23666-	
73; Berger, et al., Gene 66:1-10 (1988);	
and, Cullen, B., et al., Methods in	
 Enzymol. 216:362–368 (1992), the	
contents of each of which is herein	
incorporated by reference in its entirety.	
Adipocytes and pre-adipocytes that may be	
used according to these assays are publicly	
available (e.g., through the ATCC) and/or	
may be routinely generated. Exemplary	
cells that may be used according to these	

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				assays include the mouse 3T3-L1 cell line	
_				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
				developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
				like conversion under appropriate	
				differentiation culture conditions.	
63	HBXCX15	577	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to bind the	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factor and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	Ξ
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				A1CC). Exemplary numan 1 cells, such	indications include alicina, pancytopema, reunopema,

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as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC). Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Activation of transcription through the Signal Transducers and through the Cignal Transducers and transcription through the Signal Transducers and transcription factor of Transcription (STAT6) STAT6 response Activators of Transcription (STAT6) element in immune cells, interest and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of transcription through the STAT6 transcrip
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				275(38):29331-29337 (2000), the contents	and tissues, hemophilia, hypercoagulation, diabetes
				of each of which are herein incorporated	mellitus, endocarditis, meningitis, and Lyme Disease.
				by reference in its entirety. T cells that	Additional preferred indications include infection (e.g., an
				may be used according to these assays are	infectious disease as described below under "Infectious
				publicly available (e.g., through the	Disease").
				ATCC). Exemplary rat natural killer cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC).	
63	HBXCX15	577	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	ona
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUP1 cell line, mat may be used	Include allemia, pane y copema, reunopema,

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			according to these assays are publicly available (e.g., through the ATCC).	thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allery.
63 HBXCX15	277	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of	Highly preferred indications include blood disorders Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			which are herein incorporated by reference	immune reactions to transplanted organs and tissues,

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asthma and	NF alpha ed embodime: ed embodime: ulating (e.g., eferred indicat ed below unde orders", and/o eferred indicat matoid arthriti sease, multipl munodeficienc cell-mediated ell-mediated eferred indica disorders, and allowers, and disorders, and disorders, and disorders, and allowers, and allowers, and celferred indica disorders, and disorders, and disorders, and allowers, and lymphoma, na), solid tum atic, esophage cother preferr ve disorders a cample, a. leukopenia, a. leukopenia,
m, diabetes r me Disease,	of the invent educing) Tlighly preferr hod for stim action. Prescribe Related Dissibility preserved in the following and the following and the following and highly preserved in the following and the following and highly preserved in the following and the following
ercoagulatio mingitis, Lyv	mbodiment optiming (e.g., ralternative halternative halternative halternative halternative halternative halternative halternative halternative hune disease trythematosi as describeded below), be, and suppiese. Addition and in mage in pati ighly preferral indications lymphoma, oliferative D indications, for exampl ma (e.g., ma east, lung, colliver and ur ide benign donditions, si taplasia, and ur ide anemia, ale anemia, and ale anemia,
hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, leukopenia, leukopenia, leukopenia, leukopenia, leukopenia, leukopenia, leukopenia, leukopenia,
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at may be used re publicly ATCC). S that may be asys include the a human natura c and cytotoxic	f transcription se Element are art and may led to assess the invention agonists or any to regulate the ed in growth of growth-types. cription throug antagonists of yes disclosed in (including antagonists of ys disclosed in (1998); Culle tymol 216:362-al., Proc Natl 46 (1988); 53(9):3862-al., Virus Gene content of each orated by cells that may assays are ough the sthat may be
NK cells that ese assays a through the tan NK cell to these asse, with cytolytic	um Respon um Respon known in th mely modifi eptides of th oodies and a he invention factors and enes involv the function many cell tys for trans ay be used of t SRE activi the inventi agonists or nclude assa ene 66:1-10 thords in En- thorn et al 85:6342-63 Immunol 1 and Black et (1997), the entirety. T entirety. T engit to these ble (e.g., the
in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the
	ough slement (such cells).
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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Activation of Adipocyte ERK Signaling Pathway	NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention, including antibodies and agonists or antagonists of the invention, or or inhibit cell proliferation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and telegy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders"). Highly preferred indications include endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity", neural
141	Activation of Adipocyte ERK Signaling Pathway	Activation of Adipocyte ERK Signaling Pathway

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and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, that diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as		ameroscierosis, microvascular disease, hypericusion, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity.	Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and
be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast.	and undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation conditions known in the art.		

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					breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
49	HCDCY76	878	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular
				include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac

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hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary angiomatosis, hemangioendothelioma, lymphangiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, brain, liver, and urinary cancer. Preferred indications include benign dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis, venous and lymphatic disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include arterial disease, and Reynaud's phenomenom, aneurysms, restenosis, venous and lymphatic disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include disease, and cancer. Highly preferred indications also include disease, and cancer. Highly preferred indications also include and other vascular disease, and expendent and preferred indications also include and other vascular disease, and exp	(e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as
(bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	

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acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immannoty diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g.,
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2):
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
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	495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and	decreasing) the activation of and/or inactivating endothelial cells. A highly preferred embodiment of
	Karin, Nature 410(6824):37-40 (2001);	the invention includes a method for stimulating
	and Cobb Mrt, Frog Bropnys Mor Biol 71(3-4):479-500 (1999): the contents of	anglogements. An anemative inguity preferred canonamient of the invention includes a method for inhibiting
	each of which are herein incorporated by	angiogenesis. A highly preferred embodiment of the
	reference in its entirety. Endothelial cells	invention includes a method for reducing cardiac
	that may be used according to these assays	hypertrophy. An alternative highly preferred embodiment
	are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
	ATCC). Exemplary endothelial cells that	hypertrophy. Highly preferred indications include
	may be used according to these assays	neoplastic diseases (e.g., as described below under
	include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the
	cells (HUVEC), which are endothelial	cardiovascular system (e.g., heart disease, congestive heart
	cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyopathy,
	are involved in functions that include, but	valvular regurgitation, left ventricular dysfunction,
	are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease,
	permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
	cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
		overload, and/or as described below under
		"Cardiovascular Disorders"). Highly preferred indications
		include cardiovascular, endothelial and/or angiogenic
		disorders (e.g., systemic disorders that affect vessels such
		as diabetes mellitus, as well as diseases of the vessels
		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
-		and/or cardiovascularization. Highly preferred
		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous), glomus tumors, telangiectasia,
		bacillary angiomatosis, hemangioendothelioma,
		angiosarcoma, haemangiopericytoma, lymphangioma,
-		lymphangiosarcoma. Highly preferred indications also
		include cancers such as, prostate, breast, lung, colon,

				pancreatic, esophageal, stomach, brain, liver, and urinary
				cancer. Preferred indications include benign
				dysproliferative disorders and pre-neoplastic conditions,
				such as, for example, hyperplasia, metaplasia, and/or
				dysplasia. Highly preferred indications also include
				arterial disease, such as, atherosclerosis, hypertension,
				coronary artery disease, inflammatory vasculitides,
				Reynaud's disease and Reynaud's phenomenom,
				aneurysms, restenosis; venous and lymphatic disorders
				such as thrombophlebitis, lymphangitis, and lymphedema;
				and other vascular disorders such as peripheral vascular
				disease, and cancer. Highly preferred indications also
				include trauma such as wounds, burns, and injured tissue
				(e.g., vascular injury such as, injury resulting from balloon
				angioplasty, and atheroschlerotic lesions), implant
				fixation, scarring, ischemia reperfusion injury, rheumatoid
				arthritis, cerebrovascular disease, renal diseases such as
				acute renal failure, and osteoporosis. Additional highly
				preferred indications include stroke, graft rejection,
				diabetic or other retinopathies, thrombotic and coagulative
				disorders, vascularitis, lymph angiogenesis, sexual
				disorders, age-related macular degeneration, and treatment
				/prevention of endometriosis and related conditions.
				Additional highly preferred indications include fibromas,
				heart disease, cardiac arrest, heart valve disease, and
				vascular disease. Preferred indications include blood
				disorders (e.g., as described below under "Immune
				Activity", "Blood-Related Disorders", and/or
				"Cardiovascular Disorders"). Preferred indications include
				autoimmune diseases (e.g., rheumatoid arthritis, systemic
				lupus erythematosis, multiple sclerosis and/or as described
				below) and immunodeficiencies (e.g., as described below).
				Additional preferred indications include inflammation and
				inflammatory disorders (such as acute and chronic
				inflammatory diseases, e.g., inflammatory bowel disease
				and Crohn's disease), and pain management.
66 HCE1G78	580	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention

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includes a method for stimulating endothelial cell grown. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention) to cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred	ы ру.	these assays dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include, and cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that
n method for stimulating endouncinal ative highly preferred embodiment includes a method for inhibiting en A highly preferred embodiment of includes a method for stimulating erration. An alternative highly preferred of the invention includes a meth endothelial cell proliferation. embodiment of the invention includating apoptosis of endothelial cells. e highly preferred embodiment of th a method for inhibiting (e.g., decrea of endothelial cells.	ent of the invention includes a mething angiogenisis. An alternative high ent of the invention includes a methical angiogenesis. A highly preferrent of the invention includes a methoration hypertrophy. An alternative embodiment of the invention including cardiac hypertrophy. Highly is include neoplastic diseases (e.g., der "Hyperproliferative Disorders" of the cardiovascular system (e.g., e-heart failure, hypertension, aortice the control of the cardiovascular system (e.g., e-heart failure, hypertension, aortice the control of the cardiovascular system (e.g., e-heart failure, hypertension, aortice the control of the cardiovascular system (e.g., e-heart failure, hypertension, aortice the control of the cardiovascular system (e.g., e-heart failure, hypertension, aortice the cardiovascular system (e.g., e-heart failure, hypertension, aortice the cardiovascular system (e.g., e-heart failure) and the c	opatny, varvular regurgitation, tert on, atherosclerosis and atherosclerosis had atherosclerosis and atherosclerosis and atherosclerositabetic nephropathy, intracardiac shy, myocardial infarction, chronic, and/or as described below under ascular Disorders"). Highly preferradiovascular, endothelial and/or a ardiovascular, as well as diseases of the s, such as of the arteries, capillarie cs). Highly preferred are indication and/or cardiovascular
4)		
apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase anontosis activity	of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial	sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.
Apoptosis		

		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous), glomus tumors, telangiectasia,
		bacillary angiomatosis, hemangioendothelioma,
		angiosarcoma, haemangiopericytoma, Iymphangioma,
		lymphangiosarcoma. Highly preferred indications also
		include cancers such as, prostate, breast, lung, colon,
		pancreatic, esophageal, stomach, brain, liver, and urinary
		cancer. Preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or
		dysplasia. Highly preferred indications also include
		arterial disease, such as, atherosclerosis, hypertension,
		coronary artery disease, inflammatory vasculitides,
	· · · · · · · · · · · · · · · · · · ·	Reynaud's disease and Reynaud's phenomenom,
		aneurysms, restenosis; venous and lymphatic disorders
		such as thrombophlebitis, lymphangitis, and lymphedema;
	-	and other vascular disorders such as peripheral vascular
		disease, and cancer. Highly preferred indications also
		include trauma such as wounds, burns, and injured tissue
		(e.g., vascular injury such as, injury resulting from balloon
		angioplasty, and atheroschlerotic lesions), implant
		fixation, scarring, ischemia reperfusion injury, rheumatoid
		<u>Б</u>
		acute renal failure, and osteoporosis. Additional highly
		preferred indications include stroke, graft rejection,
		diabetic or other retinopathies, thrombotic and coagulative
		disorders, vascularitis, lymph angiogenesis, sexual
		disorders, age-related macular degeneration, and treatment
		/prevention of endometriosis and related conditions.
		Additional highly preferred indications include fibromas,
		heart disease, cardiac arrest, heart valve disease, and
		vascular disease. Preferred indications include blood

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67 HCE2H52	Upregulation of CD71 and activation of T cells	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD71, and the activation of T cells.	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease, and pain management. A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), and altimunation and inflammatory disorders. Additional highly preferred indications include infaction. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under
		Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a	"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia,

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pand dise dise dise multiple grar seps imm hem ende aller	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders (e.g., as described below under "Immune Activity") and infections (e.g., as described indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
practical approach" Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human Iymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are
	Activation of Natural Killer Cell ERK Signaling Pathway.
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				herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.	multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also prostate, brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and
69	HCE5F78	583	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992): Henthorn et al., Proc Natl	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally.

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				Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysprolliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
70	HCEDR26	584	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,
throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in
	Activation of transcription through serum response element in immune cells (such as T-cells).
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				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
	-				disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
7.2	HCEEQ25	586	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
	•			activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,

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Toutinely inoutined to assess the ability of	related Disolucis, and of caldiovascular Disolucis,
polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
proteins evaluate the production of	Additional highly preferred indications include
cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
alpha (TNFa), and the induction or	S
inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
routinely modified to test	leukemia, lymphoma, and/or as described below under
immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
 in suspension culture, which, when	Disease").
 activated by antigen and/or cytokines,	
initiate and upregulate T cell proliferation	

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				and functional activities.	
73	HCEEU18	287	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
	ü		ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
-				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	Sa
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
				cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
				and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
				like conversion under appropriate	diabetic neuropathy), blood vessel blockage, neart disease,

				differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
					blood vessel blockage), seizures, memai comusion,
					drowsiness, nonketotic hyperglycemic-nyperosmotal
					coma, cardiovascular disease (e.g., neart disease,
					atheroscierosis, microvascular disease, nypertension,
					stroke, and other diseases and disorders as described in the
					"Cardiovascular Disorders" section below), dyslipidemia,
					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infection (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below (particularly of the urinary tract
					and skin). An additional highly preferred indication is
					obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					preferred indications are complications associated with
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal systems
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include, hypertension, coronary artery disease,
		-			dyslipidemia, gallstones, osteoarthritis, degenerative
					arthritis, eating disorders, fibrosis, cachexia, and kidney
					diseases or disorders. Preferred indications include
					neoplasms and cancer, such as, lymphoma, leukemia and
					breast, colon, and kidney cancer. Additional preferred
					indications include melanoma, prostate, lung, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer.
					Highly preferred indications include lipomas and
					liposarcomas. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia.
73	HCEEU18	587	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription unlough	unough are set and response Exement	monod for minoring (v.g., rodoving) 1111 april

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	seriim resnonse element	(SBE) are well-known in the art and may	production. An alternative preferred embodiment of the
	in immine cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
	.(200	(including antibodies and agonists or	include blood disorders (e.g., as described below under
		antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
		the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
		the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
		growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
		transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
		used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
		activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
		invention (including antibodies and	immune response. Additional highly preferred indications
		agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
		include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
		Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
		Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
		Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
		85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
		Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
-		content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
		incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
		cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
		assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
		the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
		may be used according to these assays	pre-neoplastic conditions, such as, for example,
		include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
		2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
		with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			anemia (ALL), plasmacytomas, multiple myeloma,
			Burkitt's lymphoma, arthritis, AIDS, granulomatous
-			disease, inflammatory bowel disease, neutropenia,
			neutrophilia, psoriasis, suppression of immune reactions to
			transplanted organs and tissues, hemophilia,
			hypercoagulation, diabetes mellitus, endocarditis,
			meningitis, Lyme Disease, cardiac reperfusion injury, and
			asthma and allergy. An additional preferred indication
			IS INFECTION (e.g., an infectious disease as described below

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					under "Infectious Disease").
74	HCEFZ82	588	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000), and veniassen et al., J inminion	initianiniatory bower disease, sepsis, fieutropenia,

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				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
75	HCEGX05	589	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity

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be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and

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				breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
76 HCFLN88	290	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders "section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance.
		•	according to these assays are publicly	

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# 25 # 25 - 9. H	Assays for the activation of transcription Assays for the activation of transcription Well-known in the art and may be used or Well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of antibodies and agonists or antagonists of the invention) assays for transcription through the cAMP response element that may be used or response element activity of polypeptides of the include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Gene 66:1-10 (1998); Black et al., Virus Grand infection (including and infection (e.g., an infectious disease as described below under "Infectious diseases (e.g., rheumatoid andor as described below under "Infectious diseases (e.g., rheumatoid arthritis, systemic lupus erythematorsis, multiple sclerosis andor as described below under "Infectious diseases (e.g., rheumatoid andor as described below under "Infectious diseases (e.g., rheumatoid andor as described described below), inmunodeficiencies (e.g., and infection diseases (e.g., rheumatoid andor as described described below), inmunodeficiencies (e.g., and infections indications include autoimmune response, and suppressing a T cell-mediated immune response element that may be used or routinely modified to test cAMP response element activity of polypeptides of the include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Burkitt's lymphoma, and prostate, breast, lung, colon, pagonists or antagonists of the invention) agonists or antagonists of the invention) agonists or antagonists of the invention) agonists or antagonists of
available may be pancrea according according according a silet cell singer cells explained according a silet cell sexplained according a silet	Activation of Assays transcription through cAMP response routine element in immune cells (such as T-cells). CREB antibod the invergence capes wariety assays is response routine elemen inventine agonist include Gene 6 Methoc R534.
	290
	76 HCFLN88

				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the HT2	transplanted organs and tissues, hemophilia,
				cell line, which is a suspension culture of	hypercoagulation, diabetes mellitus, endocarditis,
				IL-2 dependent 1 cells that also respond to IL-4.	meningitis, Lyme Disease, and astnma and allergy.
76	HCFLN88	590	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth.	include autoimmune diseases (e.g., rheumatoid arthritis,
				Exemplary assays for transcription through	systemic lupus erythematosis, Crohn's disease, multiple
				the SRE that may be used or routinely	sclerosis and/or as described below), immunodeficiencies
				modified to test SRE activity of the	(e.g., as described below), boosting a T cell-mediated
				polypeptides of the invention (including	immune response, and suppressing a T cell-mediated
				antibodies and agonists or antagonists of	immune response. Additional highly preferred indications
				the invention) include assays disclosed in	include inflammation and inflammatory disorders, and
				Berger et al., Gene 66:1-10 (1998); Cullen	treating joint damage in patients with rheumatoid arthritis.
				and Malm, Methods in Enzymol 216:362-	An additional highly preferred indication is sepsis.
				368 (1992); Henthorn et al., Proc Natl	Highly preferred indications include neoplastic diseases
				Acad Sci USA 85:6342-6346 (1988);	(e.g., leukemia, lymphoma, and/or as described below
				Benson et al., J Immunol 153(9):3862-	under "Hyperproliferative Disorders"). Additionally,
				3873 (1994); and Black et al., Virus Genes	highly preferred indications include neoplasms and
				12(2):105-117 (1997), the content of each	cancers, such as, for example, leukemia, lymphoma,
				of which are herein incorporated by	melanoma, glioma (e.g., malignant glioma), solid tumors,
				reference in its entirety. Mouse T cells	and prostate, breast, lung, colon, pancreatic, esophageal,
				that may be used according to these assays	stomach, brain, liver and urinary cancer. Other preferred
				are publicly available (e.g., through the	indications include benign dysproliterative disorders and

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	·			ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture of T cells that also respond to IL-4.	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infentions Disease.")
12	HCFLT90	591	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,

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				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benian dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
78	HCHAB84	592	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
	_			example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar

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				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
	·			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include HITT15	
				Cells. HITT15 are an adherent epithelial	
				cell line established from Syrian hamster	
				islet cells transformed with SV40. These	
				cells express glucagon, somatostatin, and	
				glucocorticoid receptors. The cells secrete	
				insulin, which is stimulated by glucose and	
				glucagon and suppressed by somatostatin	
				or glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
79	HCMSX51	593	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	A highly preferred indication is diabetes mellitus.
			in pancreatic beta cells.	apoptosis are well known in the art and	An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,

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invention (including antibodies and	nephropathy and/or other diseases and disorders as
agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
promote caspase protease-mediated	neuropathy, nerve disease and nerve damage (e.g., due to
apoptosis. Apoptosis in pancreatic beta is	diabetic neuropathy), blood vessel blockage, heart disease,
associated with induction and progression	stroke, impotence (e.g., due to diabetic neuropathy or
of diabetes. Exemplary assays for	blood vessel blockage), seizures, mental confusion,
caspase apoptosis that may be used or	drowsiness, nonketotic hyperglycemic-hyperosmolar
routinely modified to test capase apoptosis	coma, cardiovascular disease (e.g., heart disease,
activity of polypeptides of the invention	atherosclerosis, microvascular disease, hypertension,
(including antibodies and agonists or	stroke, and other diseases and disorders as described in the
antagonists of the invention) include the	"Cardiovascular Disorders" section below), dyslipidemia,
assays disclosed in: Loweth, AC, et al.,	endocrine disorders (as described in the "Endocrine
FEBS Lett, 400(3):285-8 (1997); Saini,	Disorders" section below), neuropathy, vision impairment
KS, et al., Biochem Mol Biol Int,	(e.g., diabetic retinopathy and blindness), ulcers and
39(6):1229-36 (1996); Krautheim, A., et	impaired wound healing, and infection (e.g., infectious
al., Br J Pharmacol, 129(4):687-94 (2000);	diseases and disorders as described in the "Infectious
Chandra J, et al., Diabetes, 50 Suppl	Diseases" section below, especially of the urinary tract and
 1:S44-7 (2001); Suk K, et al., J Immunol,	skin), carpal tunnel syndrome and Dupuytren's
166(7):4481-9 (2001); Tejedo J, et al.,	contracture). An additional highly preferred
FEBS Lett, 459(2):238-43 (1999); Zhang,	indication is obesity and/or complications associated with
S., et al., FEBS Lett, 455(3):315-20	obesity. Additional highly preferred indications include
(1999); Lee et al., FEBS Lett 485(2-3):	weight loss or alternatively, weight gain. Aditional
122-126 (2000); Nor et al., J Vasc Res	highly preferred indications are complications associated
37(3): 209-218 (2000); and Karsan and	with insulin resistance.
 Harlan, J Atheroscler Thromb 3(2): 75-80	
 (1996); the contents of each of which are	
 herein incorporated by reference in its	
 entirety. Pancreatic cells that may be used	
according to these assays are publicly	
available (e.g., through the ATCC) and/or	
may be routinely generated. Exemplary	
pancreatic cells that may be used	
according to these assays include RIN-m.	
RIN-m is a rat adherent pancreatic beta	
 cell insulinoma cell line derived from a	
radiation induced transplantable rat islet	
cell tumor. The cells produce and secrete	

				islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
08	HCNC011	594	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney diseases (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. An indication are complications associated with insulin resistance.

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				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
81	HCNSD29	595	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
ļ				herein incorporated by reference in its	highly preferred indications are complications associated

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with	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious kin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred
entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J
	Regulation of viability and proliferation of pancreatic beta cells.
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indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. NS-1 NS-1 et al.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic rephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9
	Insulin Secretion
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Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a
(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity
	Activation of Adipocyte P13 Kinase Signalling Pathway
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that may be used or routinely modified to	ed to method for inhibiting adipocyte differentiation. Highly
test PI3 kinase-induced activity of	rs (e
 polypeptides of the invention (including	described below under "Endocrine Disorders").
 antibodies and agonists or antagonists of	s of Preferred indications include neoplastic diseases (e.g.,
the invention) include assays disclosed in	
Forrer et al., Biol Chem 379(8-9):1101-	
1110 (1998); Nikoulina et al., Diabetes	
49(2):263-271 (2000); and Schreyer et al.,	
 Diabetes 48(8):1662-1666 (1999), the	
contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
incorporated by reference in its entirety.	ety. Disorders"), immune disorders (e.g., as described below
Mouse adipocyte cells that may be used	
according to these assays are publicly	described below under "Neural Activity and Neurological
available (e.g., through the ATCC).	Diseases"), and infection (e.g., as described below under
Exemplary mouse adipocyte cells that may	
be used according to these assays include	lude is diabetes mellitus. An additional highly preferred
3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
mouse preadipocyte cell line that is a	
continous substrain of 3T3 fibroblast cells	
developed through clonal isolation and	
undergo a pre-adipocyte to adipose-like	
conversion under appropriate	
differentiation conditions known in the art.	
	diabetic neuropathy or blood vessel blockage), seizures,
	mental confusion, drowsiness, nonketotic hyperglycemic-
	hyperosmolar coma, cardiovascular disease (e.g., heart
	disease, atherosclerosis, microvascular disease,
	hypertension, stroke, and other diseases and disorders as
	described in the "Cardiovascular Disorders" section
	below), dyslipidemia, endocrine disorders (as described in
	the "Endocrine Disorders" section below), neuropathy,
	vision impairment (e.g., diabetic retinopathy and
	blindness), ulcers and impaired wound healing, infection
	(e.g., infectious diseases and disorders as described in the
	"Infectious Diseases" section below, especially of the
	urinary tract and skin), carpal tunnel syndrome and
	Dupuytren's contracture). An additional highly

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	-				preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia,
83	жоссон жения жени	597	Regulation of transcription through the PEPCK promoter in hepatocytes	Assays for the regulation of transcription through the PEPCK promoter are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the PEPCK promoter in a reporter construct and regulate liver gluconeogenesis. Exemplary assays for regulation of transcription through the PEPCK promoter that may be used or routinely modified to test for PEPCK promoter activity (in hepatocytes) of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine

Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., an infectious diseases or disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuvtren's	contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include glycogen storage disease (e.g., glycogenoses), hepatitis, gallstones, cirrhosis of the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and cholesterol metabolism, and hepatocarcinomas. Highly preferred indications	rders (e.g., "Cardiov,", "Cardiov,"), inder "Imm der "Imm se and/or d Disease"), e der "Endo described b biscaribed b	neoplastic dise rproliferative I neoplasms and state, breast, lu ach, brain, and is is liver cancer. benign dysprol
Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Lochhead et al., Diabetes 49(6):896-903 (2000); and Yaazlev et al., J Biol Chem	of each of which is herein incorporated by reference in its entirety. Hepatocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary liver hepatoma cells that may	be used according to these assays include H4lle cells, which contain a tyrosine amino transferase that is inducible with glucocorticoids, insulin, or cAMP derivatives.		

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					disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
83	96ЭЭЭЭН	597	Activation of Skeletal	Kinase assay. Kinase assays, for examplek	Highly preferred indications include endocrine
			Muscle Cell EKK Signalling Pathway	EIK-1 Kinase assays, for EKK signal transduction that regulate cell proliferation	disorders (e.g., as described below under Endocrine Disorders") and disorders of the musculoskeletal system.
			f=	or differentiation are well known in the art	Preferred indications include neoplastic diseases (e.g., as
				and may be used or routinely modified to	described below under "Hyperproliferative Disorders"),
				assess the ability of polypeptides of the	blood disorders (e.g., as described below under "Immune
				invention (including antibodies and	Activity", "Cardiovascular Disorders", and/or "Blood-
				agonists or antagonists of the invention) to	Related Disorders"), immune disorders (e.g., as described
				promote or inhibit cell proliferation,	below under "Immune Activity"), neural disorders (e.g., as
				activation, and differentiation. Exemplary	described below under "Neural Activity and Neurological
				assays for ERK kinase activity that may be	ou (e
				used or routinely modified to test ERK	<u>ښ</u>
				kinase-induced activity of polypeptides of	is diabetes mellitus. An additional highly preferred
				the invention (including antibodies and	indication is a complication associated with diabetes (e.g.,
				agonists or antagonists of the invention)	diabetic retinopathy, diabetic nephropathy, kidney disease
				include the assays disclosed in Forrer et	(e.g., renal failure, nephropathy and/or other diseases and
				al., Biol Chem 379(8-9):1101-1110	disorders as described in the "Renal Disorders" section
				(1998); Le Marchand-Brustel Y, Exp Clin	below), diabetic neuropathy, nerve disease and nerve
				Endocrinol Diabetes 107(2):126-132	damage (e.g., due to diabetic neuropathy), blood vessel
				(1999); Kyriakis JM, Biochem Soc Symp	blockage, heart disease, stroke, impotence (e.g., due to
				64:29-48 (1999); Chang and Karin, Nature	diabetic neuropathy or blood vessel blockage), seizures,
	-			410(6824):37-40 (2001); and Cobb MH,	mental confusion, drowsiness, nonketotic hyperglycemic-
				Prog Biophys Mol Biol 71(3-4):479-500	hyperosmolar coma, cardiovascular disease (e.g., heart
				(1999); the contents of each of which are	disease, atherosclerosis, microvascular disease,
				herein incorporated by reference in its	hypertension, stroke, and other diseases and disorders as
				entirety. Rat myoblast cells that may be	described in the "Cardiovascular Disorders" section
				used according to these assays are publicly	below), dyslipidemia, endocrine disorders (as described in
				available (e.g., through the ATCC).	the "Endocrine Disorders" section below), neuropathy,
				Exemplary rat myoblast cells that may be	vision impairment (e.g., diabetic retinopathy and
				used according to these assays include L6	blindness), ulcers and impaired wound healing, infection
				cells. L6 is an adherent rat myoblast cell	(e.g., infectious diseases and disorders as described in the
				line, isolated from primary cultures of rat	"Infectious Diseases" section below, especially of the
				thigh muscle, that fuses to form	pal
				multinucleated myotubes and striated	Dupuytren's contracture). An additional highly
				Hoers after culture in differentiation media.	preferred indication is obesity and/or complications

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					associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Highly preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as,
84	нсосл56	865	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described

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indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating RANTES production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) RANTES production. A highly preferred indication is infectious Disease"). A most highly preferred below under "Infectious Disease"). A most highly preferred indication includes AIDS and/or the prevention or reduction of HIV infection. Additional highly preferred indication includes immune disorders, for example, inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed
	Production of RANTES
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	HCQCM24
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				the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response	pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune
				element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or	diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), hoosting a T cell-mediated immune response, and
				antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992);	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis,
				are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used	"Infectious Disease as described Derow under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia,
				according to these assays are publicly available (e.g., through the ATCC).	thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and
88	HCRNF78	602	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune

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chronic hyperproliterative diseases.	Activity, Blood-Related Disorders, and/or
Assays for immunomodulatory and differentiation factor proteins produced by	Cardiovascular Disorders), and infection (e.g., as described below under "Infectious Disease"). Highly
 a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
 expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
or routinely modified to assess the ability	preferred indications also include boosting a B cell-
of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
the invention) to mediate	indications include inflammation and inflammatory
immunomodulation and differentiation and	disorders. Additional highly preferred indications include
modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
 agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
 include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
 assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
disclosed herein or otherwise known in the	described below under "Infectious Disease").
art. Human dendritic cells are antigen	
presenting cells in suspension culture,	
which, when activated by antigen and/or	

				cytokines, initiate and upregulate T cell	
68	HCUAF85	603	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benigm dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include include inflammation and inflammatory disorders.
ક	HCI ICE89	604	Protection from	HELA cell line.	A highly preferred embodiment of the invention
2	HUUULEON	DU4	Protection from	Caspase Apoptosis Kescue. Assays for	A highly preferred embodiment of the invention

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	Endothelial Cell	caspase apoptosis rescue are well known in	caspase apoptosis rescue are well known in includes a method for stimulating endothelial cell growth.
	Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
		modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
		polypeptides of the invention (including	growth. A highly preferred embodiment of the
		antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
		the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
		mediated apoptosis. Exemplary assays for	embodiment of the invention includes a method for
		caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
		routinely modified to test caspase	preferred embodiment of the invention includes a method
		apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
		invention (including antibodies and	highly preferred embodiment of the invention includes a
-		agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
		include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
		al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
		Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
		1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
		Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
		each of which are herein incorporated by	embodiment of the invention includes a method for
		reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
		that may be used according to these assays	embodiment of the invention includes a method for
	•	are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
		commercial sources). Exemplary	embodiment of the invention includes a method for
		endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
		according to these assays include bovine	preferred embodiment of the invention includes a method
		aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
		an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
		blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
		that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
		angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
		vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
		extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
	-		disease, diabetic nephropathy, intracardiac shunt, cardiac
			hypertrophy, myocardial infarction, chronic hemodynamic
			overload, and/or as described below under
			"Cardiovascular Disorders"). Highly preferred
			indications include cardiovascular, endothelial and/or
			angiogenic disorders (e.g., systemic disorders that affect

	vessels such as diabetes mellitus, as well as diseases of the
	vessels themselves, such as of the arteries, capillaries,
	veins and/or lymphatics). Highly preferred are indications
	that stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,
	coronary artery disease, inflammatory vasculitides,
	Reynaud's disease and Reynaud's phenomenom,
	aneurysms, restenosis; venous and lymphatic disorders
	such as thrombophlebitis, lymphangitis, and lymphedema;
	and other vascular disorders such as peripheral vascular
	disease, and cancer. Highly preferred indications also
	include trauma such as wounds, burns, and injured tissue
	(e.g., vascular injury such as, injury resulting from balloon
	 angioplasty, and atheroschlerotic lesions), implant
	 fixation, scarring, ischemia reperfusion injury, rheumatoid
	 arthritis, cerebrovascular disease, renal diseases such as
	acute renal failure, and osteoporosis. Additional highly
	preferred indications include stroke, graft rejection,
	diabetic or other retinopathies, thrombotic and coagulative
	disorders, vascularitis, lymph angiogenesis, sexual
	disorders, age-related macular degeneration, and treatment

Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease, and pain management.	ays for caspase Preferred embodiments of the invention include using polypeptides of the invention) to modified to and podies and bodies and motocal tissues are mucosal tissues and mast cells are mucosal tissues. Il apoptosis may ease and mast cell avokines, is an allergic disease. Il apoptosis may be used or t capase apoptosis of the bodies and fithe invention) and the invention of the invention in the art and mast cell avokines, is an allergic disease. Il apoptosis may be used or t capase apoptosis of the bodies and fithe invention)
	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assessed disclosed in Masuda A
	Regulation of apoptosis of immune cells (such as mast cells).
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				et al., J Biol Chem. 276(28):26107-26113	
				(2001): Yeatman CF 2nd. et al I Exn	
				Med. 192(8):1093-1103 (2000):Lee et al.	
				FEBS Lett 485(2-3): 122-126 (2000); Nor	
-				et al., J Vasc Res 37(3): 209-218 (2000);	
				and Karsan and Harlan, J Atheroscler	
				Thromb 3(2): 75-80 (1996); the contents of	
				each of which are herein incorporated by	
				reference in its entirety. Immune cells that	
				may be used according to these assays are	
				publicly available (e.g., through	
				commercial sources). Exemplary immune	
				cells that may be used according to these	
				assays include mast cells such as the HMC	
				human mast cell line.	
H 16	HCUCK44	909	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
			Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth.
			Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
				modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
				polypeptides of the invention (including	growth. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
				the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
				mediated apoptosis. Exemplary assays for	embodiment of the invention includes a method for
				caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
				routinely modified to test caspase	preferred embodiment of the invention includes a method
				apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
				invention (including antibodies and	highly preferred embodiment of the invention includes a
				agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
	·			include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
				al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
				Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
				1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
				Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred
	•			each of which are herein incorporated by	embodiment of the invention includes a method for
				reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
				that may be used according to these assays	embodiment of the invention includes a method for
				are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred

commercial sources). Exemplary	embodiment of the invention includes a method for
endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
according to these assays include bovine	preferred embodiment of the invention includes a method
aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
	disease, diabetic nephropathy, intracardiac shunt, cardiac
	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred
	indications include cardiovascular, endothelial and/or
	angiogenic disorders (e.g., systemic disorders that affect
	vessels such as diabetes mellitus, as well as diseases of the
	vessels themselves, such as of the arteries, capillaries,
	veins and/or lymphatics). Highly preferred are indications
	that stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,

					coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom,
				-	aneurysms, restenosis; venous and lymphatic disorders
					such as thrombophlebitis, lymphangitis, and lymphedema;
					$\overline{}$
					disease, and cancer. Highly preferred indications also
					include trauma such as wounds, burns, and injured tissue
					(e.g., vascular injury such as, injury resulting from balloon
					angioplasty, and atheroschlerotic lesions), implant
					fixation, scarring, ischemia reperfusion injury, rheumatoid
					al d
					acute renal failure, and osteoporosis. Additional highly
					preferred indications include stroke, graft rejection,
	·				diabetic or other retinopathies, thrombotic and coagulative
					disorders, vascularitis, lymph angiogenesis, sexual
					disorders, age-related macular degeneration, and treatment
					/prevention of endometriosis and related conditions.
	·		****		Additional highly preferred indications include fibromas,
					heart disease, cardiac arrest, heart valve disease, and
			-1-4-4		vascular disease. Preferred indications include blood
					disorders (e.g., as described below under "Immune
					Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
91	HCUCK44	605	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				moderned by a large vertical of call, and not	miciates a method for stimulating (e.g., meteasing) Med -1
				to induce chemotoxic and activation of	the invention includes a method for inhibiting (e.g.
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional

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				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	
	-			dendritic cells are antigen presenting cells	
				in suspension culture, which, when	
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
92	HCUDD64	909	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed	A highly preferred embodiment of the invention
	-			by activated T cells, macrophages,	includes a method for stimulating the production of GM-
				endothelial cells, and fibroblasts. GM-	CSF. An alternative highly preferred embodiment of the

CSF regulates differentiation and	invention includes a method for inhibiting the production
proliferation of granulocytes- macrophage	of GM-CSF. Highly preferred indications include
progenitors and enhances antimicrobial	inflammation and inflammatory disorders. An additional
 activity in neutrophils, monocytes and	highly preferred indication is infection (e.g., as described
macrophage. Additionally, GM-CSF plays	below under "Infectious Disease". Highly preferred
an important role in the differentiation of	indications include blood disorders (e.g., neutropenia (and
dendritic cells and monocytes, and	the prevention of neutropenia (e.g., in HIV infected
increases antigen presentation. GM-CSF	patients), and/or as described below under "Immune
is considered to be a proinflammatory	Activity", "Blood-Related Disorders", and/or
cytokine. Assays for immunomodulatory	"Cardiovascular Disorders"). Highly preferred indications
proteins that promote the production of	also include autoimmune diseases (e.g., rheumatoid
 GM-CSF are well known in the art and	arthritis, systemic lupus erythematosis, multiple sclerosis
may be used or routinely modified to	and/or as described below) and immunodeficiencies (e.g.,
assess the ability of polypeptides of the	as described below). Additional highly preferred
invention (including antibodies and	indications include asthma. Highly preferred indications
agonists or antagonists of the invention) to	include neoplastic diseases (e.g., leukemia (e.g., acute
mediate immunomodulation and modulate	lymphoblastic leukemia, and acute myelogenous
the growth and differentiation of	leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and
leukocytes. Exemplary assays that test for	Hodgkin's disease), and/or as described below under
immunomodulatory proteins evaluate the	"Hyperproliferative Disorders"). Highly preferred
production of cytokines, such as GM-CSF,	indications include neoplasms and cancers, such as,
and the activation of T cells. Such assays	leukemia, lymphoma, melanoma, and prostate, breast,
that may be used or routinely modified to	lung, colon, pancreatic, esophageal, stomach, brain, liver
test immunomodulatory activity of	and urinary cancer. Other preferred indications include
polypeptides of the invention (including	benign dysproliferative disorders and pre-neoplastic
antibodies and agonists or antagonists of	conditions, such as, for example, hyperplasia, metaplasia,
 the invention) include the assays disclosed	and/or dysplasia. Highly preferred indications include:
in Miraglia et al., J Biomolecular	suppression of immune reactions to transplanted organs
Screening 4:193-204 (1999); Rowland et	and tissues (e.g., bone marrow transplant); accelerating
 al., "Lymphocytes: a practical approach"	myeloid recovery; and mobilizing hematopoietic
 Chapter 6:138-160 (2000); and Ye et al., J	progenitor cells. Preferred indications include boosting
Leukoc Biol (58(2):225-233, the contents	a T cell-mediated immune response, and alternatively,
of each of which are herein incorporated	suppressing a T cell-mediated immune response.
by reference in its entirety. Natural killer	Preferred indications include anemia, pancytopenia,
cells that may be used according to these	leukopenia, thrombocytopenia, acute lymphocytic anemia
assays are publicly available (e.g., through	(ALL), plasmacytomas, multiple myeloma, Burkitt's
the ATCC) or may be isolated using	lymphoma, arthritis, AIDS, granulomatous disease,

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92 HCUDD64	909	Regulation of apoptosis in pancreatic beta cells.	techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity. Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,
			assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80	endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.

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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications
test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):2366-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cells that may be used according to these assays include the mouse 3T3-L1 cell sare a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Activation of transcription through serum response element in immune cells (such as T-cells).
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				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to bind the	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factor and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
_				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
	-			and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary human T cells, such	indications include anemia, pancytopenia, leukopenia,
				as the MOLT4, that may be used according	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	-			to these assays are publicly available (e.g.,	anemia (ALL), plasmacytomas, multiple myeloma,
				through the ATCC).	Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
93	HCWAE64	209	Activation of transcription through	Assays for the activation of transcription through the Signal Transducers and	A highly preferred indication is allergy. Another highly preferred indication is asthma
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			STAT6 response	Activators of Transcription (STAT6)	highly preferred indications include inflammation and
			element in immune	response element are well-known in the art	inflammatory disorders. Preferred indications
			cells (such as natural	and may be used or routinely modified to	include blood disorders (e.g., as described below under
			killer cells).	assess the ability of polypeptides of the	"Immune Activity", "Blood-Related Disorders", and/or
				invention (including antibodies and	"Cardiovascular Disorders"). Preferred indications include
				agonists or antagonists of the invention) to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				regulate STAT6 transcription factors and	lupus erythematosis, multiple sclerosis and/or as described
				modulate the expression of multiple genes.	below) and immunodeficiencies (e.g., as described below).
				Exemplary assays for transcription through	Preferred indications include neoplastic diseases (e.g.,
				the STAT6 response element that may be	leukemia, lymphoma, melanoma, and/or as described
				used or routinely modified to test STAT6	below under "Hyperproliferative Disorders"). Preferred
				response element activity of the	indications include neoplasms, such as, for example,
				polypeptides of the invention (including	leukemia, lymphoma, melanoma, and prostate, breast,
				antibodies and agonists or antagonists of	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the invention) include assays disclosed in	and urinary cancer. Other preferred indications include
				Berger et al., Gene 66:1-10 (1998); Cullen	benign dysproliferative disorders and pre-neoplastic
				and Malm, Methods in Enzymol 216:362-	conditions, such as, for example, hyperplasia, metaplasia,
				368 (1992); Henthorn et al., Proc Natl	and/or dysplasia. Preferred indications include
				Acad Sci USA 85:6342-6346 (1988);	anemia, pancytopenia, leukopenia, thrombocytopenia,
				Georas et al., Blood 92(12):4529-4538	Hodgkin's disease, acute lymphocytic anemia (ALL),
				(1998); Moffatt et al., Transplantation	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				69(7):1521-1523 (2000); Curiel et al., Eur	arthritis, AIDS, granulomatous disease, inflammatory
				J Immunol 27(8):1982-1987 (1997); and	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				Masuda et al., J Biol Chem	suppression of immune reactions to transplanted organs
				275(38):29331-29337 (2000), the contents	and tissues, hemophilia, hypercoagulation, diabetes
				of each of which are herein incorporated	mellitus, endocarditis, meningitis, and Lyme Disease.
				by reference in its entirety. T cells that	Additional preferred indications include infection (e.g., an
				may be used according to these assays are	infectious disease as described below under "Infectious
				publicly available (e.g., through the	Disease").
				ATCC). Exemplary rat natural killer cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC).	
93	HCWAE64	209	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
				Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for

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			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
			-	the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
*				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
·					immune reactions to transplanted organs and tissues,
		36			hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
93	HCWAE64	209	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			INFAI response	ceils (INFA1) response element are well-	Biood-Kelated Disorders, and/or Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			Cons (such as natural	toutinery infomined to assess the ability of	autominimie diseases (e.g., incumatora al mins, systemic

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			Alife Collo).	antibodies and agonists or antagonists of	helow) imminodeficiencies (e.g., as described helow)
				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
				expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
-				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
			-	response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
		··.		Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Aramburu et al., J	such as, for example, hyperplasia, metaplasia, and/or
				Exp Med 182(3):801-810 (1995); De Boer	dysplasia. Preferred indications also include anemia,
				et al., Int J Biochem Cell Biol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				31(10):1221-1236 (1999); Fraser et al., Eur	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				J Immunol 29(3):838-844 (1999); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Yeseen et al., J Biol Chem 268(19):14285-	granulomatous disease, inflammatory bowel disease,
				14293 (1993), the contents of each of	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				which are herein incorporated by reference	immune reactions to transplanted organs and tissues,
				in its entirety. NK cells that may be used	hemophilia, hypercoagulation, diabetes mellitus,
				according to these assays are publicly	endocarditis, meningitis, Lyme Disease, asthma and
				available (e.g., through the ATCC).	allergy.
				Exemplary human NK cells that may be	
	-			used according to these assays include the	
				NK-YT cell line, which is a human natural	
				killer cell line with cytolytic and cytotoxic	
				activity.	
3	HCWAE64	209	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
	:		as liatulai kilici celisj.	ability of polypeptides of the invention	increasing) Line alpha production. Preferred indications

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				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
94	HCWFU39	809	Upregulation of CD71 and activation of T cells	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An
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				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
95	HCWUL09	609	Activation of	Assays for the activation of transcription	A highly preferred indication includes allergy. A
			transcription through	through the GATA3 response element are	#
,			GATA-3 response	well-known in the art and may be used or	preferred indication includes rhinitis. Additional highly
ı			element in immune	routinely modified to assess the ability of	preferred indications include infection (e.g., an infectious
			cells (such as T-cells).	polypeptides of the invention (including	disease as described below under "Infectious Disease"),
				antibodies and agonists or antagonists of	and inflammation and inflammatory disorders.
			•	the invention) to regulate GATA3	Preferred indications include blood disorders (e.g., as
				transcription factors and modulate	described below under "Immune Activity", "Blood-
				expression of genes important for Th2	Related Disorders", and/or "Cardiovascular Disorders").
		-		immune response development.	Preferred indications include autoimmune diseases (e.g.,
				Exemplary assays for transcription through	rheumatoid arthritis, systemic lupus erythematosis,
				the GATA3 response element that may be	multiple sclerosis and/or as described below) and
		,		used or routinely modified to test GATA3-	immunodeficiencies (e.g., as described below).
				response element activity of polypeptides	Preferred indications include neoplastic diseases (e.g.,
				of the invention (including antibodies and	leukemia, lymphoma, melanoma, and/or as described
				agonists or antagonists of the invention)	below under "Hyperproliferative Disorders"). Preferred
				include assays disclosed in Berger et al.,	indications include neoplasms and cancer, such as, for
				Gene 66:1-10 (1998); Cullen and Malm,	example, leukemia, lymphoma, melanoma, and prostate,
				Methods in Enzymol 216:362-368 (1992);	breast, lung, colon, pancreatic, esophageal, stomach,
				Henthorn et al., Proc Natl Acad Sci USA	brain, liver and urinary cancer. Other preferred indications
				85:6342-6346 (1988); Flavell et al., Cold	include benign dysproliferative disorders and pre-
				Spring Harb Symp Quant Biol 64:563-571	neoplastic conditions, such as, for example, hyperplasia,
				(1999); Rodriguez-Palmero et al., Eur J	metaplasia, and/or dysplasia. Preferred indications
				Immunol 29(12):3914-3924 (1999); Zheng	include anemia, pancytopenia, leukopenia,
				and Flavell, Cell 89(4):587-596 (1997);	thrombocytopenia, leukemias, Hodgkin's disease, acute
				and Henderson et al., Mol Cell Biol	lymphocytic anemia (ALL), plasmacytomas, multiple
				14(6):4286-4294 (1994), the contents of	myeloma, Burkitt's lymphoma, arthritis, AIDS,
		,		each of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. T cells that may	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				be used according to these assays are	immune reactions to transplanted organs and tissues,
				publicly available (e.g., through the	hemophilia, hypercoagulation, diabetes mellitus,
				ATCC). Exemplary mouse T cells that	endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays	
				include the H12 cell line, which is a	

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				suspension culture of IL-2 dependent T cells that also respond to IL-4.	
96	HDHAA42	610	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using	role in the immune system and is	includes a method for stimulating the production of IFNg.
			Natural Killer cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the invention includes a marked for inhibiting the production
				inhibits TH2; promotes IgG2a and inhibits	of IFNg. Highly preferred indications include blood
				IgE; induces macrophage activation; and	disorders (e.g., as described below under "Immune
				increases MHC expression. Assays for	Activity", "Blood-Related Disorders", "Hyperproliferative
				immunomodulatory proteins produced by	Disorders" (e.g. cancer/tumorigenesis) and/or
				T cells and NK cells that regulate a variety	"Cardiovascular Disorders"), and infection (e.g., viral
				of inflammatory activities and inhibit TH2	infections, tuberculosis, infections associated with chronic
				helper cell functions are well known in the	granulomatosus disease and malignant osteoporosis,
				art and may be used or routinely modified	and/or as described below under "Infectious Disease").
				to assess the ability of polypeptides of the	Highly preferred indications include autoimmune disease
				invention (including antibodies and	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				agonists or antagonists of the invention) to	multiple sclerosis and/or as described below),
				mediate immunomodulation, regulate	immunodeficiency (e.g., as described below), boosting a T
				inflammatory activities, modulate TH2	cell-mediated immune response, and suppressing a T cell-
				helper cell function, and/or mediate	mediated immune response, boosting antibody-dependent
				humoral or cell-mediated immunity.	immune responses, suppressing antibody-dependent
				Exemplary assays that test for	immune responses, boosting innate immunity and immune
				immunomodulatory proteins evaluate the	responses, and suppressing innate immunity and immune
				production of cytokines, such as Interferon	responses. Additional highly preferred indications include
,				gamma (IFNg), and the activation of T	inflammation and inflammatory disorders. Additional
				cells. Such assays that may be used or	preferred indications include idiopathic pulmonary
				routinely modified to test	fibrosis. Highly preferred indications include neoplastic
				immunomodulatory activity of	diseases (e.g., leukemia, lymphoma, melanoma, and/or as
				polypeptides of the invention (including	described below under "Hyperproliferative Disorders").
				antibodies and agonists or antagonists of	Highly preferred indications include neoplasms and
				the invention) include the assays disclosed	cancers, such as, for example, leukemia, lymphoma,
				in Miraglia et al., J Biomolecular	melanoma, and prostate, breast, lung, colon, pancreatic,
				Screening 4:193-204 (1999); Rowland et	esophageal, stomach, brain, liver and urinary cancer.
				al., "Lymphocytes: a practical approach"	Other preferred indications include benign dysproliferative
				Chapter 6:138-160 (2000); Gonzalez et al.,	disorders and pre-neoplastic conditions, such as, for
				J Clin Lab Anal 8(5):225-233 (1995);	example, hyperplasia, metaplasia, and/or dysplasia.
				Dilliau et al., Ailli IN I Acad Sci 630:22-32	rreierred indications include anemia, pancytopenia,

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(1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Natural Killer (NK) cells that may be used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind amtigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgB production and has strong effects on B cells. IL-6 participates in IL-4 induced IgB production. An alternative highly preferred embodiment of participates in IL-4 induced IgB production (IgA plays a reducing) IL-6 production. An alternative highly preferred embodiment of production (IgA plays a reducing) IL-6 production. An inglihy preferred embodiment of mucosal information of IL-6 has been linked to autoimmune diseases. Assays for immunomodulatory and a large variety of cells where the expression level is strongly regulated by preferred indications include autoimmune diseases (e.g., expression level is strongly regulated by preferred indications include autoimmune diseases (e.g., expression level is strongly regulated by preferred indications include autoimmune diseases (e.g., expression level is strongly regulated by preferred indications include autoimmune diseases (e.g., expression level is strongly regulated by preferred indications include autoimmune diseases (e.g., as described below) and are well known in the art and may be used or routinely modified to assess the ability preferred indications also include boosting a B cell-andiated immune response. Highly preferred indications and all antibodies and agonists or antagonists of indications include autoimmune diseases (e.g., as described below) and are well known in the art and may be used or routinely modified to assess the ability and indications are include boosting a B cell-andiated immune response. Highly preferred indications and inflammatory and indications produced inflammation and inflammatory
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				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for immunomodulatory proteins evaluate the	neopiasue diseases (e.g., niyeroma, piasmaeyroma, leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	=
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
86	HDPCW16	612	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
		*		may be used or routinely modified to	-3
				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
		,		agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
				mediate immunomodulation, modulate	Cardiovascular Disorders). migniy preferred indications

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				chemotaxis and modulate T cell	include autoimmune diseases (e.g. rheumatoid arthritis
				differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
				for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
				the production of chemokines, such as	described below). Additional highly preferred indications
				macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
				monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
				modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
86	HDPCW16	612	Production of ICAM-1	Assays for measuring expression of	Preferred embodiments of the invention include using
				ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
				may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
				assess the ability of polypeptides of the	and/or treatment of Inflammation, Vascular Disease,
				invention (including antibodies and	Athereosclerosis, Restenosis, and Stroke

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to y n l l l l l l l l l l l l l l l l l l	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indication is sepsis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and
agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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				Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
100	HDPDJ58	614	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for simulating the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described

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Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred

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indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively predominantly on cells that are actively predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the ard may be used or routinely modified to assays the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the immunomodulatory proteins evaluate the inflammation and inflammatory disorders. Additional highly preferred indications include infection. Preferred upregulation of cell surface markers, such assays that may be used or routinely modified to test immunomodulatory proteins evaluate the indications include evaluate the inflammation and inflammatory disorders. Additional highly preferred indications include infection. Preferred upregulation of cell surface markers, such assays that may be used or routinely modified to test immunomodulatory proteins evaluate the indications include infection indications include infection. Preferred indications include infection indications include evaluate the inferior including and inflammatory disorders. Additional highly preferred indications include infection. Preferred indications include infection indications include assays that may be used or routinely include neoplasms and cancers. Such assays that may be used or routinely includence in the proteins evaluate the indications include ind
	Upregulation of T cells receptor and activation of T cells receptor carryin prolifer predom prolifer immun activate prolifer and ma assess inventi agonist mediate immun immun upregu as CD7
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			activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus,
			Human T cells are primary human I cells are primary human I lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	endocardius, meninglus, Lyme Disease, and astinna and allergy.
101 HDPFF10	615	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders.

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				monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
				modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
243				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
102	HDPFU43	919	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly

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			a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
			expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
			cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
-			are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
			or routinely modified to assess the ability	preferred indications also include boosting a B cell-
			of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
			antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
			the invention) to mediate	indications include inflammation and inflammatory
			immunomodulation and differentiation and	disorders. Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
			diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
			the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
			agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
			include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
			J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
			a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
			(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
			158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
			each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
			reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
			cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
			assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
			disclosed herein or otherwise known in the	described below under "Infectious Disease").
		•	art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
+			proliferation and functional activities.	
102 HDPFU43	616	Activation of Skeletal	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention

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blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulerers and impaired wound healing, infections (e.g., infectious diseases and disorders as described in the "Infectious Disoases" section below, especially of the urinary tract and skin), carpal turnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications include weight loss or alternatively, weight gain. Additional highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, thabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benian	dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	eins produced by includes a method for inhibiting (e.g., decreasing) TNF T cells, fibroblasts, alpha production. An alternative highly preferred embodiment of the invention includes a method for
		TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that
		Production of TNF alpha by dendritic cells
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exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
well known in the art and may be used or	as described below under "Immune Activity", "Blood-
routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
 assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
proteins evaluate the production of	Additional highly preferred indications include
cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
alpha (TNFa), and the induction or	<u>:</u>
inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
routinely modified to test	leukemia, lymphoma, and/or as described below under
immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
 Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
 be used according to these assays may be	ij
isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
In Suspension culture, when	Discase).

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				activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	
103	HDPFY18	617	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, elifammatory bowel disease, scute lymphocytic aneutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
103	HDPFY18	617	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a

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Other preferred indications include benign dysproliferative "Cardiovascular Disorders"), Highly preferred indications method for inhibiting the activation of and/or inactivating below), boosting a T cell-mediated immune response, and systemic lupus erythematosis, multiple sclerosis and/or as blood disorders (e.g., as described below under "Immune proliferation. An alternative highly preferred embodiment described below), immunodeficiencies (e.g., as described leukopenia, thrombocytopenia, Hodgkin's disease, acute reactions to transplanted organs and tissues, hemophilia, of the invention includes a method for stimulating T cell include autoimmune diseases (e.g., rheumatoid arthritis, Highly preferred indications include neoplastic diseases melanoma, and prostate, breast, lung, colon, pancreatic, An Highly preferred indications include (e.g., leukemia, lymphoma, and/or as described below lymphocytic anemia (ALL), plasmacytomas, multiple esophageal, stomach, brain, liver and urinary cancer. under "Hyperproliferative Disorders"). Additionally, disorders and pre-neoplastic conditions, such as, for granulomatous disease, inflammatory bowel disease, cancers, such as, for example, leukemia, lymphoma, Preferred indications include anemia, pancytopenia, sepsis, neutropenia, neutrophilia, psoriasis, immune example, hyperplasia, metaplasia, and/or dysplasia. highly preferred indications include neoplasms and additional preferred indication is infection (e.g., as A highly preferred embodiment of the hypercoagulation, diabetes mellitus, endocarditis, invention includes a method for inhibiting T cell suppressing a T cell-mediated immune response. inflammatory disorders, and asthma and allergy. myeloma, Burkitt's lymphoma, arthritis, AIDS, described below under "Infectious Disease"). Activity", "Blood-Related Disorders", and/or meningitis, Lyme Disease, inflammation and proliferation. CD8+ T cells are well known in the art and expressed almost exclusively on CD4+ and agonists or antagonists of the invention) to 77(1):1-10 (1999); Oostervegal et al., Curr et al., J Biomolecular Screening 4:193-204 proliferation. Reduced CD152 expression the maintenance of T cell homeostasis and upregulation of cell surface markers, such Opin Immunol 11(3):294-300 (1999); and are herein incorporated by reference in its autoimmune diseases. Overexpression of immunomodulatory proteins important in 321 (1998), the contents of each of which immunity. Exemplary assays that test for Such assays that may be used or routinely example, the assays disclosed in Miraglia entirety. Human T cells that may be used according to these assays may be isolated has been linked to hyperproliferative and immunomodulatory proteins evaluate the (1999); Rowland et al., "Lymphocytes: a (2000); McCoy et al., Immunol Cell Biol antagonists of the invention) include, for activity of polypeptides of the invention Saito T, Curr Opin Immunol 10(3):313as CD152, and the activation of T cells. practical approach" Chapter 6:138-160 assess the ability of polypeptides of the may be used or routinely modified to (including antibodies and agonists or modified to test immunomodulatory invention (including antibodies and maintain T cell homeostasis, and/or modulate the activation of T cells, mediate humoral or cell-mediated immunoresponses. Assays for CD152 may lead to impaired

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		:	using techniques disclosed herein or	
		-	otherwise known in the art. Human I cells	
			are primary human lymphocytes that	
			mature in the thymus and express a T Cell	
			receptor and CD3, CD4, or CD8. These	
			cells mediate humoral or cell-mediated	
			immunity and may be preactivated to	
-			enhance responsiveness to	
			immunomodulatory factors.	
104 HDPGE24	618	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			are well-known in the art and may be used	An additional highly preferred indication is a complication
			or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
			of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
			antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
			pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
			glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
			proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
			key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
			assays that may be used or routinely	stroke, and other diseases and disorders as described in the
			modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
			secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
			polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
			Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
			(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
			Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
			Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
			865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
-			Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
			Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
			Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
			of each of which is herein incorporated by	with insulin resistance.

reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian harnster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. 1784 78, 433-6443, 1981	Pregulation of Malic Enzyme are well-known in the art in the partocytes assess the ability of polypeptides of the regulate transcription of Malic Enzyme are well-known in the art in the patocytes assess the ability of polypeptides of the invention of regulate transcription of Malic Enzyme as agonists or antagonists of the invention of regulate transcription of Malic Enzyme are well-known in the art in the patocytes as a genists or antagonists of the invention of the promoter may also response elements. ME promoter may also responds to API and other transcription of Malic Enzyme, assays that may be used or routinely modified to test for regulation of Malic Enzyme, and additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy and/or other diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, and diabetic retinopathy, and associated with diabetes (e.g., diabetic retinopathy and viorat regulation of promoter may also responds to API and other transcription of Malic Enzyme assays that may be used or routinely modified to test for regulation of e.g., diabetic retinopathy and blindness), ulcers and tisorders as described in the architecturing and tisorders and disorders as a complication of malic enzyme in lipogenesisand its expression is stimulted by insulin. ME promoter promoter may also responds elements. ME architecture described in the architecture and other transcription of Malic Enzyme (e.g., diabetic returnopathy, vision impairment (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsines, nonketotic hypergrays or dispersion, and other diseases and disorders as described in the architecture and other diseases and disorders and disorders and disorders and disorders as elements. ME architecture and other diseases and disorders are complication of malic enzyment and promoter architecture and disorders and disorders are calcinopation of malic f
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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating hepatocyte cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating hepatocyte cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell differentiation. A highly preferred embodiment of the invention includes a method for activating hepatocyte cells. An alternative
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J Biol Chem, 274(25):17997-8004 (1999); Jipenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse 3T3-L1 cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	Activation of Hepatocyte ERK Signaling Pathway
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with the contents of the patients of the liver and/or embridge and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) described below under "Endocrine Disorders"). Highly preferred indications include neoplastic diseases (e.g., as described below under "Thyperpoliferative Disorders"). 4.10(682-91.101-1110) 4.29-48 (1999); Chang and Karin, Nature described below under "Thyperpoliferative Disorders"). 4.10(682-91.37-40 (2001); and Cobb MH. Activity", "Cardiovascular Disorders" (e.g., as described below under "Immune disorders (e.g	
used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat liver hepatoma cells that may be used according to these assays include H4lle cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.	used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat liver hepatoma cells that may be used according to these assays include H4lle cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.

complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hepatitis, jaundice, gallstones, cirrhosis of the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and chlolesterol metabolism. Additional highly preferred indications include neoplasms and cancers, such as, hepatocarcinomas, other liver cancers, and colon and pancreatic cancer. Preferred indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	
	Kinase assays, for example an Elk-1 kinase assay for ERK signal transduction that regulates cell proliferation or differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Ali H, et al., J Immunol, 165(12):7215-7223 (2000);
	Regulation of proliferation and/or differentiation in immune cells (such as mast cells).
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Tam SY, et al., Blood, 90(5):1807-1820 (1997); Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells that may be used according to these assays include human mast cells such as the HMC-1 cell line.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory considered to be a proinflammatory considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes TH3 and inhibits TH2 differentiation; promotes are inhibits TH2 differentiation; promotes and inhibits TH2 differentiation; and increases and inhibits TH2 differentiation; and increases and immunomodulatory proteins produced by art and may be used or routinely modified to assess the ability of polypeptides of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 cells and Nt cells that regulate a variety are at and may be used or routinely modified to assess the ability of polypeptides of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 difformations include inflammatory activities, modulate TH2 disorders. Additional preferred indications include inflammatory disorders. Additional preferred indications include response, and suppressing a T cell-mediated immunity. Exemplary assays that test for the invention include neoplastic disease (e.g., interpretation and or cell-mediated immunity. Interpretation and inflammatory disorders disorders. Additional preferred indications include helper real indications include neoplastic disease (e.g., interpretation and indications include indiparting the production of IFNg. An alternative including antibodies and disorders. Additional preferred indications include indiparting the production of IFNg. Interpretation including antibodies and disorders. Additional preferred indications include indiparting the production of IFNg. Interpretation includes a m
	Production of IFN gamma using a T ro cells collinia in in im in the collinia in
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	HDPIU94
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indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and premeaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or
gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from
	Insulin Secretion
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	HDPOC24
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	pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
	glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
	proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
	key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
	assays that may be used or routinely	stroke, and other diseases and disorders as described in the
	modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
	secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
	polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
	antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
	the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
	Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
	(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
	Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
	Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
	865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
	Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
	Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
	Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
	of each of which is herein incorporated by	with insulin resistance.
	reference in its entirety. Pancreatic cells	
	that may be used according to these assays	
	are publicly available (e.g., through the	
	ATCC) and/or may be routinely generated.	
	Exemplary pancreatic cells that may be	
	used according to these assays include	
	HITT15 Cells. HITT15 are an adherent	
	epithelial cell line established from Syrian	
	hamster islet cells transformed with SV40.	
	These cells express glucagon,	
	somatostatin, and glucocorticoid receptors.	
	The cells secrete insulin, which is	
	stimulated by glucose and glucagon and	
	suppressed by somatostatin or	
	glucocorticoids. ATTC# CRL-1777	
	Refs: Lord and Ashcroft. Biochem. J. 219:	
-	547-551; Santerre et al. Proc. Natl. Acad.	
	Sci. USA 78: 4339-4343, 1981.	

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				RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980	
,	HDPOL37	621	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., I Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indication is sepsis. An additional highly preferred indication include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and indications include benign dysproliferative disorders and

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				publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below and as "Infection Carting Disease").
108	HDP0076	622	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Teals that may be used according to these	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, melanoma, glioma (e.g., malignant glioma), solid tumors,

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assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL—hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou or disease.").	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-bolypeptides of the invention to promote or inhibit may be used or routinely modified to assess for PI3 kinase activity of est PI3 kinase-induced activity of est PI3 kinase-induced activity of en invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-Forrer et al., Biol Chem 379(8-9):1101-G1988); Nikoulina et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein
assays are publicly available (e.g., thro the ATCC). Exemplary mouse T cells may be used according to these assays include the CTLL cell line, which is an 2 dependent suspension culture of T ce with cytotoxic activity.	Kinase assay. Kinase assays, for examplan GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability o polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et a Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein
	Activation of Adipocyte Pl3 Kinase Signalling Pathway
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	incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly	Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Disorder"), and infention (e.g., as described below under
	available (e.g., through the A1CC). Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1
	be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent	is diabetes menitus. An additional inginy preferred indication is a complication associated with diabetes (e.g.,
	mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
	continous substrain of 31.3 fibroblast cells developed through clonal isolation and	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section
	undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
	conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
	differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
		mantal confusion, drowsiness, nonketotic hyperglycemic-
		hyperosmolar coma, cardiovascular disease (e.g., heart
		disease, atherosclerosis, microvascular disease,
		hypertension, stroke, and other diseases and disorders as
-		described in the "Cardiovascular Disorders" section
		below), dyslipidemia, endocrine disorders (as described in
		the "Endocrine Disorders" section below), neuropathy,
		vision impairment (e.g., diabetic retinopathy and
		blindness), ulcers and impaired wound healing, infection
		(e.g., infectious diseases and disorders as described in the
		"Infectious Diseases" section below, especially of the
		rpal
		Dupuytren's contracture). An additional highly
		preferred indication is obesity and/or complications
		indications include weight loss or afternatively weight
		minications include weight toss of aircringurery, weight
		complications associated with insulin resistance.
		Additional highly preferred indications are disorders of the
		musculoskeletal systems including myopathies, muscular
		dystrophy, and/or as described herein.
		Additional highly preferred indications include,
		hypertension, coronary artery disease, dyslipidemia,

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gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Activation of transcription and transcription intrough through the API response element are in immune cells (such propriete of the invention (including as T-cells). API response element are routinely modified to assess the ability of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the API response element are rangeousiss of the invention) to modulate growth and element that may be used or routinely modified to test API -response element activity of polyypeptides of the invention) include and agonists of the invention include and adolise and agonists of the invention include and agonists of the invention include and ABIII a
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				to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T	bower disease, sepsis, psoriasis, suppression or minimie reactions to transplanted organs and tissues, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the HT2 cell line, which is	
				an IL-2 dependent suspension culture cell	
				line that also responds to IL-4.	
601	НОРРО93	623	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	well-known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
			-	transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
				Human T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
				to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
				through the ATCC). Exemplary human T	reactions to transplanted organs and tissues, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the SUPT cell line, which is	
				an IL-2 and IL-4 responsive suspension-	

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				culture cell line.	
92	нрррп93	623	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
}) 	transcription through	through the CD28 response element are	includes a method for stimulating T cell proliferation. An
			CD28 response element	well-known in the art and may be used or	alternative highly preferred embodiment of the invention
	_		in immune cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation. A
			as T-cells).	polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
				the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
				in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
				transcription through the CD28 response	A highly preferred embodiment of the invention includes a
				element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
				modified to test CD28-response element	An alternative highly preferred embodiment of the
				activity of polypeptides of the invention	sa
				(including antibodies and agonists or	IL-2 production. Additional highly preferred
				antagonists of the invention) include	indications include inflammation and inflammatory
				assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
				66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
				Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
				85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
		_		Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. Highly
				(1997); Parra et al., J Immunol	preferred indications include neoplastic diseases (e.g.,
				166(4):2437-2443 (2001); and Butscher et	melanoma, renal cell carcinoma, leukemia, lymphoma,
				al., J Biol Chem 3(1):552-560 (1998), the	and/or as described below under "Hyperproliferative
				contents of each of which are herein	Disorders"). Highly preferred indications include
				incorporated by reference in its entirety. T	neoplasms and cancers, such as, for example, melanoma
				cells that may be used according to these	(e.g., metastatic melanoma), renal cell carcinoma (e.g.,
			-	assays are publicly available (e.g., through	metastatic renal cell carcinoma), leukemia, lymphoma
				the ATCC). Exemplary human T cells that	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
				may be used according to these assays	pancreatic, esophageal, stomach, brain, liver and urinary
				include the SUPT cell line, which is a	cancer. Other preferred indications include benign
				suspension culture of IL-2 and IL-4	dysproliferative disorders and pre-neoplastic conditions,
				responsive T cells.	such as, for example, hyperplasia, metaplasia, and/or
					dysplasia. A highly preferred indication includes
					infection (e.g., AIDS, tuberculosis, infections associated
					with granulomatous disease, and osteoporosis, and/or as
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preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Diseases"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, and/or
	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al.,
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
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				biochim biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4	dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
109	HDPPD93	623	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred

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			each of which are herein incorporated by reference in its entirety. T cells that may	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
			ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
			may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
			include the SUP1 cell line, which is a	suppression of immune reactions to transplanted organs,
			suspension culture of IL-2 and IL-4 responsive T cells.	asthma and allergy.
109 HDPPD93	623	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
		transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
		NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
		element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
		cells (such as natural	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
		killer cells).	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
			antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
			the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
			transcription factors and modulate	suppressing a T cell-mediated immune response.
			expression of genes involved in	Additional highly preferred indications include
			immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
			assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
			response element that may be used or	disease as described below under "Infectious Disease").
			routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
			element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
			invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
••			agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
			include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
			Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
			Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
			Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
			85:6342-6346 (1988); Aramburu et al., J	such as, for example, hyperplasia, metaplasia, and/or
			Exp Med 182(3):801-810 (1995); De Boer	dysplasia. Preferred indications also include anemia,
			et al., Int J Biochem Cell Biol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
			31(10):1221-1236 (1999); Fraser et al., Eur	disease, acute lymphocytic anemia (ALL), plasmacytomas,
			J Immunol 29(3):838-844 (1999); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
			Yeseen et al., J Biol Chem 268(19):14285-	granulomatous disease, inflammatory bowel disease,
			14293 (1993), the contents of each of	sepsis, neutropenia, neutrophilia, psoriasis, suppression of

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			which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
110 HDPPQ30	30 624	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, hood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious Diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include weight loss or alternatively, weight gain. Additional
			nerein incorporated by reference in its entirety. Pancreatic cells that may be used	highly preferred indications are complications associated with insulin resistance.

				according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	
HDH TIII	HDPPW82	625	Upregulation of CD71 and activation of T cells		A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include infection. Preferred indications include infection. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver lung, colon, pancreatic, esophageal, stomach, brain, liver

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				chemotaxis activity of polypeptides of the invention (including antibodies and	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Blomolecular Screening 4:193-	
				204(1999); Rowland et al., Lymphocytes: a practical approach. Chapter 6:138-160	alletgy. Preferred indications also include fleopiastic diseases (e.g., lenkemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
112	HDPXN20	626	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	incl
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),

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invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
inflammatory activities, modulate TH2	indications include inflammation and inflammatory
 helper cell function, and/or mediate	disorders. Additional preferred indications include
 humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
 Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
 immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
polypeptides of the invention (including	include benign dysproliferative disorders and pre-
antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
 the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
 Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
 of each of which are herein incorporated	
by reference in its entirety. Human T cells	
 that may be used according to these assays	
may be isolated using techniques disclosed	
herein or otherwise known in the art.	
Human T cells are primary human	
lymphocytes that mature in the thymus and	
express a T Cell receptor and CD3, CD4,	
or CD8. These cells mediate humoral or	
cell-mediated immunity and may be	
preactivated to enhance responsiveness to	
immunomodulatory factors.	

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113 HDQHM36	627	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, plood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance.	
			Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian		
			hamster islet cells transformed with SV40.		

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			These cells express glucagon,	
			somatostatin, and glucocorticoid receptors.	
			The cells secrete insulin, which is	
			stimulated by glucose and glucagon and	
			suppressed by somatostatin or	
			glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
			Sci. USA 78: 4339-4343, 1981.	
114 HDTAU35	628	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
			and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
			participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
			and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
			role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
			cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
			of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
			disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
			chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
			Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
			differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
			a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
			expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
			cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
			are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
			or routinely modified to assess the ability	preferred indications also include boosting a B cell-
			of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
			antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
			the invention) to mediate	indications include inflammation and inflammatory
			immunomodulation and differentiation and	disorders. Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.

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Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely
	Production of MIP1alpha
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			modified to test immunomodulatory and chemotaxis activity of polypeptides of the	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
			invention (including antibodies and agonists or antagonists of the invention)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
			include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
			J Biomolecular Screening 4:193-	
			204(1999); Kowland et al., Lymphocytes: a practical approach" Chapter 6:138-160	anergy. Treferred minicanons and include neoplasme diseases (e.g., leukemia, lymphoma, and/or as described
			(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
			Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
			al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
			Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
			2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
			Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
			each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
			reference in its entirety. Human dendritic	dysplasia.
			cells that may be used according to these	
			assays may be isolated using techniques	
			disclosed herein or otherwise known in the	
			art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
			proliferation and functional activities.	
114 HDTAU35	628	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
		alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
			activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
			smooth muscle, and other cell types that	embodiment of the invention includes a method for
			exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
			cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
			well known in the art and may be used or	as described below under "Immune Activity", "Blood-
			routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
			polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
			antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
			the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
	٠		immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
			inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and

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				assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, menincitis, Lyme Disease, cardiac
			·	isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
115	HDTAV54	629	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g.,

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well known in the art and may be used of	As described below under minimum creating, process
routinely modified to assess the ability of	Kelated Disorders, and/or Cardiovascular Disorders /,
polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
proteins evaluate the production of	Additional highly preferred indications include
cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
alpha (TNFa), and the induction or	Ś
 inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
routinely modified to test	leukemia, lymphoma, and/or as described below under
immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
 160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
 herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
in suspension culture, which, when	Disease").
activated by antigen and/or cytokines,	
initiate and upregulate T cell proliferation	

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				and functional activities.	
116	HDTFX18	630	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			•	or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
	-			invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	ss a
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
-				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
		-		entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
,				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
		_		cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
				and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
				like conversion under appropriate	diadeuc neuropauny), blood vessel blockage, near disease,

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				differentiation conditions buown in the art	stroke impotence (e.g. due to diabetic neuropathy or
					blood vessel blockage), seizures, mental confusion,
•					drowsiness, nonketotic hyperglycemic-hyperosmolar
					coma, cardiovascular disease (e.g., heart disease,
					atherosclerosis, microvascular disease, hypertension,
					stroke, and other diseases and disorders as described in the
					"Cardiovascular Disorders" section below), dyslipidemia,
					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
-					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infection (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below (particularly of the urinary tract
		,			and skin). An additional highly preferred indication is
					obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					preferred indications are complications associated with
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal systems
					including myopathies, muscular dystrophy, and/or as
				•	described herein. Additional highly preferred
					indications include, hypertension, coronary artery disease,
					dyslipidemia, gallstones, osteoarthritis, degenerative
					arthritis, eating disorders, fibrosis, cachexia, and kidney
-					diseases or disorders. Preferred indications include
					neoplasms and cancer, such as, lymphoma, leukemia and
					breast, colon, and kidney cancer. Additional preferred
					indications include melanoma, prostate, lung, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer.
					Highly preferred indications include lipomas and
					liposarcomas. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia.
1117	HDTGW48	631	Activation of transcription through	Assays for the activation of transcription through the NFKB response element are	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or

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antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh B-cell line.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and
NFKB response element in immune cells (such as B-cells).	Production of MIP1alpha
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may be used or routinely modified to	(e.g. an infections disease as described below under
assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
invention (including antibodies and	blood disorders (e.g., as described below under "Immune
agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
the production of chemokines, such as	described below). Additional highly preferred indications
macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
 assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
reference in its entirety. Human dendritic	dysplasia.
cells that may be used according to these	
assays may be isolated using techniques	
disclosed herein or otherwise known in the	
art. Human dendritic cells are antigen	
 presenting cells in suspension culture,	
 which, when activated by antigen and/or	
cytokines, initiate and upregulate T cell	
proliferation and functional activities.	

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A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated	inmune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and
Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.
Activation of transcription through serum response element in immune cells (such as T-cells).	
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					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
119	HE2CA60	633	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate R cells. The cells	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of
				macrophages and mast cells and promote	the invention includes a method for inhibiting (e.g.,
				polarization of CD4+ cells into 1Hz cells are well known in the art and may be used	reducing) 1L-4 production. A nignly preferred indication includes asthma. A highly preferred
				or routinely modified to assess the ability of nolymentides of the invention (including	indication includes allergy. A highly preferred indication includes rhinitis Additional highly preferred
				antibodies and agonists or antagonists of	iati
				the invention) to mediate immune immune stimulate immune	disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma,
				cells, modulate immune cell polarization,	melanoma, and/or as described below under
				and/or mediate humoral or cell-mediated	"Hyperproliferative Disorders"). Preferred indications
				immunity. Exemplary assays that test for immunomodulatory profeins evaluate the	include neoplasms and cancers, such as, for example,
				production of cytokines, such as IL-4, and	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the stimulation of immune cells, such as B	and urinary cancer. Other preferred indications include
				cells, T cells, macrophages and mast cells.	benign dysproliferative disorders and pre-neoplastic
				Such assays that may be used or routinely	s, fo
				modified to test immunomodulatory	and/or dysplasia. Preferred indications include blood
,				activity of polypeptides of the invention (including antibodies and agonists or	disorders (e.g., as described below under 'Immune Activity'. "Blood-Related Disorders'. and/or
				antagonists of the invention) include the	"Cardiovascular Disorders"). Preferred indications include
				assays disclosed in Miraglia et al., J	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Biomolecular Screening 4:193-204 (1999);	lupus erythematosis, multiple sclerosis and/or as described
				Rowland et al., "Lymphocytes: a practical	below) and immunodeficiencies (e.g., as described below).
				approach Chapter 6:138-100 (2000);	Preferred indications include anemia, pancytopenia,
				283 (1194): Vssel et al. Res Imminol	l'europeina, infoliocytopeina, frougain s'usease, acute Ivmphoevtie anemia (ALI) plasmaevtomas, multiple
				144(8):610-616 (1993); Bagley et al., Nat	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Immunol 1(3):257-261 (2000); and van der	granulomatous disease, inflammatory bowel disease,
				Graaff et al., Rheumatology (Oxford)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				38(3):214-220 (1999), the contents of each of which are herein incorporated by	immune reactions to transplanted organs and tissues, hemonitia hymercoamlation diabetes mellitus
				Of Willeli are incledin incorporated by	IICHIOPHINA, IIJPOINOABUIANOII, MINUNINA IIINIINAS,

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			that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
120 HE2CA60	634	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred

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				inay be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	hyperplastic conditions, such as, for example, hyperplastic conditions, and/or dysplastia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
120	HE2CA60	634	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes allergy. A highly preferred indication includes rhinitis. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include Activity", "Blood-Related Disorders", and/or

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			· ·	assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
121	HE2CH58	635	Activation of transcription through GAS response element in epithelial cells (such as HELA cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include include include inflammation and inflammatory disorders.

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(including antibodies and agonists or antagonists of the invention) include assays disclosed in: You M, et al., J Biol Chem, 272(37):23376-2338 (1997); Min W, et al., Circ Res, 83(8):815-823 (1998); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell line.	Regulation of transcription transcription transcription via through the DMEF1 response element in adjocytes and pre-adjocytes and pre-adjocytes and pre-adjocytes and pre-adjocytes polypeptides of the invention) to activate the DMEF1 response element is prosent in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin and binds to MEF2 transcription factor that is required for insulin responsive glucose transporter in fat and muscle tissue. Exemplary assays
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impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.		A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival.
that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells underen a pre-adipocyte to adipocyte	like conversion under appropriate differentiation culture conditions.	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-
		Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway
		637
		HE2HC60
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known in the art and may be used or	A preferred embodiment of the invention includes a
routinely modified to assess the ability of	method for stimulating muscle cell proliferation. In a
polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is
antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
 Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
that may be used or routinely modified to	of the invention includes a method for stimulating muscle
test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
polypeptides of the invention (including	muscle cell differentiation is stimulated. An alternative
antibodies and agonists or antagonists of	highly preferred embodiment of the invention includes a
the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
available (e.g., through the ATCC).	described below under "Immune Activity",
Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus. An
multinucleated myotubes and striated	additional highly preferred indication is a complication
fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g, due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,

					atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia.
					endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and important the infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below, especially of the urinary tract and
					tun
					is obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					preferred indications are complications associated with
					insulin resistance. Additonal highly preferred
					indications are disorders of the musculoskeletal system
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include: myopathy, atrophy, congestive heart
					failure, cachexia, myxomas, fibromas, congenital
					e, c
					heart valve disease, and vascular disease. Highly
					preferred indications include neoplasms and cancer, such
					as, rhabdomyoma, rhabdosarcoma, stomach, esophageal,
					prostate, and urinary cancer. Preferred indications also
					include breast, lung, colon, pancreatic, brain, and liver
					cancer. Other preferred indications include benign
	•				dysproliferative disorders and pre-neoplastic conditions,
					such as, hyperplasia, metaplasia, and/or dysplasia.
124	HE2PO93	638	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Dothusse Orginaling	the modern of the factorial of a language	distinction tight another of the increase
			ratilway	nansunction that regulate glucose	IIOII
				metabolism and cell survival are well-	includes a method for decreasing adipocyte survival. A
				known in the art and may be used or	preferred embodiment of the invention includes a method
			-	routinely modified to assess the ability of	for stimulating adipocyte proliferation. An alternative
				polypeptides of the invention (including	highly preferred embodiment of the invention includes a

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	antibodies and agonists or antagonists of the invention) to promote or inhibit	method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method
	glucose metabolism and cell survival.	for stimulating adipocyte differentiation. An alternative
	Exemplary assays for PI3 kinase activity	ıcln
	that may be used or routinely modified to	method for inhibiting adipocyte differentiation. Highly
	test PI3 kinase-induced activity of	preferred indications include endocrine disorders (e.g., as
	polypeptides of the invention (including	described below under "Endocrine Disorders").
	antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
	the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
	Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
	1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
	49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
	Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
	contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
	incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
	Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
	according to these assays are publicly	described below under "Neural Activity and Neurological
	available (e.g., through the ATCC).	Diseases"), and infection (e.g., as described below under
	Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication
	be used according to these assays include	is diabetes mellitus. An additional highly preferred
	3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
	mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
	continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
	developed through clonal isolation and	disorders as described in the "Renal Disorders" section
	undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
	conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
	differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
		diabetic neuropathy or blood vessel blockage), seizures,
		mental confusion, drowsiness, nonketotic hyperglycemic-
		hyperosmolar coma, cardiovascular disease (e.g., heart
-		disease, atherosclerosis, microvascular disease,
		hypertension, stroke, and other diseases and disorders as
		described in the "Cardiovascular Disorders" section
		below), dyslipidemia, endocrine disorders (as described in
		the "Endocrine Disorders" section below), neuropathy,
		vision impairment (e.g., diabetic retinopathy and
		blindness), ulcers and impaired wound healing, infection

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				(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include melanoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
124 HE2P093	638	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated

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				wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
				agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
				include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary
				85:6342-6346 (1988); Black et al., Virus	cancer. Other preferred indications include benign
				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions,
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia,
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the	transplanted organs and tissues, hemophilia,
				CTLL cell line, which is a suspension	hypercoagulation, diabetes mellitus, endocarditis,
				culture of IL-2 dependent cytotoxic T	meningitis, Lyme Disease, and asthma and allergy.
				cells.	
125	HE6AU52	639	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,

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				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
	····			presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
125	HE6AU52	639	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred

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	smooth muscle, and other cell types that	embodiment of the invention includes a method for
	exert a wide variety of inflammatory and	stimulating (e.g., increasing) INF alpha production.
	cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
	well known in the art and may be used or	as described below under "Immune Activity", "Blood-
	routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
	polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
	antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
	immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
	inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
	assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
	proteins evaluate the production of	Additional highly preferred indications include
	cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
	alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
-	inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
	response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
	routinely modified to test	leukemia, lymphoma, and/or as described below under
	immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
	polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
	antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
	the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
	Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
	4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
	"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
	Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
	al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
	(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
	160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
-	al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
	Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
	(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
	herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
	entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
	be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
	isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
	or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
	dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious

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				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation and functional activities.	
126	HE6CS65	640	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
	,			participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
	•			differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute

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lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes
204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include
	Production of MCP-1
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	·			assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation	mellitus, endocarditis, meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
127	HE6D092	1.	Production of MIP1alpha	immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein I alpha (MIP-1a), and the activation of	A fightly preferred embodiffied to the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, barboaria, theorytopenia, disease a sourte
					lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,

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				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
•				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
128	HE6EY13	642	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described

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below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic retinopathy, diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, attoke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,
activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the
	Regulation of apoptosis in pancreatic beta cells.
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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the
assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1980 777:3519.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Endothelial Cell Apoptosis
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	HE6FV29
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	agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
	promote caspase protease-mediated	cell proliferation. An alternative nignily preferred
	apoptosis. Induction of apoptosis in	metne
	endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A filgnly
	of tumors is associated with tumor	preferred embodiment of the invention includes a method
	regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
	supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
	apoptosis that may be used or routinely	1g (e.g
	modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
	of polypeptides of the invention (including	embodiment of the invention includes a method for
	antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
	the invention) include the assays disclosed	embodiment of the invention includes a method for
	in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
	(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
	218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
	Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
	the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
	incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
	Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
	according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
	available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
	sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
	may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
	include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
	(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
-	endothelial cells which line blood vessels	overload, and/or as described below under
	and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
	but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
	vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
	immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
-		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal

disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis, venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

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					limis erythematosis multiple sclerosis and/or as described
-					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bower disease and Crohn's disease), and pain management.
130	HE6FV29	644	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	tunne
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
-				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	

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			pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
131 HE8FC45	645	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below, boosting a proliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic,

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				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
•				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
-				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
•				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				anhance reconnectiveness to	
				cinialice responsiveness to	
133	UE8EC45	979	I Inremigation of CD152	CD152 FMAT CD152 (a k a CTI A 4)	A highly preferred embodiment of the invention
101	C+2 10711	2		expression is restricted to activated T cells	includes a method for activating T cells. An alternative
			מווס מכוו גמווסוו מו ד כמווס	CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	n in
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications

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	may be used or routinely modified to	include autoimmine diseases (e.g., rheumatoid arthritis,
	assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
	invention (including antibodies and	described below), immunodeficiencies (e.g., as described
	agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
	modulate the activation of T cells,	suppressing a T cell-mediated immune response.
	maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
	mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
	immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
	immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
	upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
	as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
	Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
	modified to test immunomodulatory	Other preferred indications include benign dysproliferative
	activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
	(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
	antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
	example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
	(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
	practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
	(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
-	77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
	Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
	Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
	321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
	are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
	entirety. Human T cells that may be used	described below under "Infectious Disease").
	according to these assays may be isolated	
	using techniques disclosed herein or	
	otherwise known in the art. Human T cells	
	are primary human lymphocytes that	
	mature in the thymus and express a T Cell	
	receptor and CD3, CD4, or CD8. These	
	cells mediate humoral or cell-mediated	
	immunity and may be preactivated to	
	enhance responsiveness to	
	immunomodulatory factors.	

A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and	impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
	the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt. 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of in Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain
Stimulation of insulin secretion from pancreatic beta cells.	
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				characteristics typical of native nancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
134	HE8FD92	648	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	tunne
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	cations i
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	

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				cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
\dashv				Endocrinology 1992 130;167.	
135 H	HE8FD92	649	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
		•		insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
·				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
·				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	

				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
136	HE8FD92	650	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
	.==			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
			-	proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			-	the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
			-	Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include

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		·	herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	highly preferred indications are complications associated with insulin resistance.
137 HE8FD92	651	Stimulation of insulin secretion from pancreatic beta cells.		A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic retinopathy, highest disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, holood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious diseases" section below, senecially of the urinary trart and

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skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.
	Production of ICAM-1
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				Cells that may be used according to these assays are publicly available (e.g., through	
				the ATCC) and/or may be routinely generated. Exemplary cells that may be	
				used according to these assays include	
				Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	
139	HE8TY46	653	Activation of	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Hepatocyte ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating hepatocyte cell
			Signaling Pathway	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting
				and may be used or routinely modified to	hepatocyte cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating hepatocyte cell differentiation. An alternative
				agonists or antagonists of the invention) to	highly preferred embodiment of the invention includes a
				promote or inhibit cell proliferation,	method for inhibiting hepatocyte cell differentiation. A
				activation, and differentiation. Exemplary	highly preferred embodiment of the invention includes a
				assays for ERK kinase activity that may be	method for activating hepatocyte cells. An alternative
				used or routinely modified to test ERK	highly preferred embodiment of the invention includes a
				kinase-induced activity of polypeptides of	method for inhibiting the activation of and/or inactivating
				the invention (including antibodies and	hepatocyte cells. Highly preferred indications include
				agonists or antagonists of the invention)	disorders of the liver and/or endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Preferred indications include neoplastic diseases (e.g., as
				(1998); Kyriakis JM, Biochem Soc Symp	described below under "Hyperproliferative Disorders"),
				64:29-48 (1999); Chang and Karin, Nature	blood disorders (e.g., as described below under "Immune
				410(6824):37-40 (2001); and Cobb MH,	Activity", "Cardiovascular Disorders", and/or "Blood-
				Prog Biophys Mol Biol 71(3-4):479-500	Related Disorders"), immune disorders (e.g., as described
				(1999); the contents of each of which are	below under "Immune Activity"), neural disorders (e.g., as
				herein incorporated by reference in its	described below under "Neural Activity and Neurological
				entirety. Rat liver hepatoma cells that may	Diseases"), and infection (e.g., as described below under
				be used according to these assays are	"Infectious Disease"). A highly preferred
				publicly available (e.g., through the	indication is diabetes mellitus. An additional highly
				ATCC). Exemplary rat liver hepatoma	preferred indication is a complication associated with
				cells that may be used according to these	diabetes (e.g., diabetic retinopathy, diabetic nephropathy,
				assays include H4lle cells, which are	kidney disease (e.g., renal failure, nephropathy and/or
				known to respond to glucocorticoids,	other diseases and disorders as described in the "Renal

	insulin or cAMP derivatives	Disorders" section below), diabetic neuronathy, nerve
		disease and nerve damage (e.g., due to diabetic
		neuropathy), blood vessel blockage, heart disease, stroke,
		impotence (e.g., due to diabetic neuropathy or blood vessel
		blockage), seizures, mental confusion, drowsiness,
		nonketotic hyperglycemic-hyperosmolar coma,
		cardiovascular disease (e.g., heart disease, atherosclerosis,
		microvascular disease, hypertension, stroke, and other
		diseases and disorders as described in the "Cardiovascular
		Disorders" section below), dyslipidemia, endocrine
		disorders (as described in the "Endocrine Disorders"
		section below), neuropathy, vision impairment (e.g.,
		diabetic retinopathy and blindness), ulcers and impaired
		wound healing, infection (e.g., infectious diseases and
		disorders as described in the "Infectious Diseases" section
		below, especially of the urinary tract and skin), carpal
		tunnel syndrome and Dupuytren's contracture). An
		additional highly preferred indication is obesity and/or
		complications associated with obesity. Additional highly
		preferred indications include weight loss or alternatively,
		weight gain. Additional highly preferred indications
		are complications associated with insulin resistance.
		Additional highly preferred indications are disorders of the
		musculoskeletal systems including myopathies, muscular
		dystrophy, and/or as described herein.
		Additional highly preferred indications include, hepatitis,
		jaundice, gallstones, cirrhosis of the liver, degenerative or
		necrotic liver disease, alcoholic liver diseases, fibrosis,
	-	liver regeneration, metabolic disease, dyslipidemia and
		chlolesterol metabolism. Additional highly
		preferred indications include neoplasms and cancers, such
-		as, hepatocarcinomas, other liver cancers, and colon and
		pancreatic cancer. Preferred indications also include
		prostate, breast, lung, esophageal, stomach, brain, and
		urinary cancer. Other preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or

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					dysplasia.
140	HE9CY05	654	Activation of	Assays for the activation of transcription	A highly preferred indication includes allergy. A
			transcription through	through the GATA3 response element are	highly preferred indication includes asthma. A highly
			GATA-3 response	well-known in the art and may be used or	preferred indication includes rhinitis. Additional highly
			element in immune	routinely modified to assess the ability of	preferred indications include infection (e.g., an infectious
			cells (such as T-cells).	polypeptides of the invention (including	disease as described below under "Infectious Disease"),
				antibodies and agonists or antagonists of	and inflammation and inflammatory disorders.
				the invention) to regulate GATA3	Preferred indications include blood disorders (e.g., as
				transcription factors and modulate	described below under "Immune Activity", "Blood-
				expression of genes important for Th2	Related Disorders", and/or "Cardiovascular Disorders").
				immune response development.	Preferred indications include autoimmune diseases (e.g.,
				Exemplary assays for transcription through	rheumatoid arthritis, systemic lupus erythematosis,
				the GATA3 response element that may be	multiple sclerosis and/or as described below) and
				used or routinely modified to test GATA3-	immunodeficiencies (e.g., as described below).
				response element activity of polypeptides	Preferred indications include neoplastic diseases (e.g.,
				of the invention (including antibodies and	leukemia, lymphoma, melanoma, and/or as described
			-	agonists or antagonists of the invention)	below under "Hyperproliferative Disorders"). Preferred
				include assays disclosed in Berger et al.,	indications include neoplasms and cancer, such as, for
				Gene 66:1-10 (1998); Cullen and Malm,	example, leukemia, lymphoma, melanoma, and prostate,
				Methods in Enzymol 216:362-368 (1992);	breast, lung, colon, pancreatic, esophageal, stomach,
				Henthorn et al., Proc Natl Acad Sci USA	brain, liver and urinary cancer. Other preferred indications
				85:6342-6346 (1988); Flavell et al., Cold	include benign dysproliferative disorders and pre-
				Spring Harb Symp Quant Biol 64:563-571	neoplastic conditions, such as, for example, hyperplasia,
				(1999); Rodriguez-Palmero et al., Eur J	metaplasia, and/or dysplasia. Preferred indications
				Immunol 29(12):3914-3924 (1999); Zheng	include anemia, pancytopenia, leukopenia,
				and Flavell, Cell 89(4):587-596 (1997);	thrombocytopenia, leukemias, Hodgkin's disease, acute
				and Henderson et al., Mol Cell Biol	lymphocytic anemia (ALL), plasmacytomas, multiple
				14(6):4286-4294 (1994), the contents of	myeloma, Burkitt's lymphoma, arthritis, AIDS,
	***			each of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. T cells that may	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				be used according to these assays are	immune reactions to transplanted organs and tissues,
				publicly available (e.g., through the	hemophilia, hypercoagulation, diabetes mellitus,
				ATCC). Exemplary mouse T cells that	endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays	
				include the HT2 cell line, which is a	
				suspension culture of IL-2 dependent T	
				cells that also respond to IL-4.	

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141 HE9EA10	655	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with insulin resistance. Altitional highly preferred indications associated with insulin resistance.
			according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics twoical of native pancreatic	

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				beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992, 130:167.	
142	HE9GG20	656	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
143	HEBCI18	657	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").

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				routinely modified to test NFAT-response	Preferred indications include neonlastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
			-	Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
				ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the SUPT cell line, which is a	
				suspension culture of IL-2 and IL-4	
				responsive T cells.	
144	HEBCY54	658	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription through	through the FAS promoter element are	An additional highly preferred indication is a complication
			the FAS promoter	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in hepatocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the FAS	neuropathy, nerve disease and nerve damage (e.g., due to
				promoter element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				and to regulate transcription of FAS, a key	stroke, impotence (e.g., due to diabetic neuropathy or
				enzyme for lipogenesis. FAS promoter is	blood vessel blockage), seizures, mental confusion,
				regulated by many transcription factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				including SREBP. Insulin increases FAS	coma, cardiovascular disease (e.g., heart disease,
				gene transcription in livers of diabetic	atherosclerosis, microvascular disease, hypertension,

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				mice. This stimulation of transcription is	stroke, and other diseases and disorders as described in the
				also somewhat glucose dependent.	"Cardiovascular Disorders" section below), dyslipidemia,
				Exemplary assays that may be used or	endocrine disorders (as described in the "Endocrine
				routinely modified to test for FAS	Disorders" section below), neuropathy, vision impairment
				promoter element activity (in nepatocytes)	(e.g., diabetic retinopathy and bilindness), dicers and
				antibodies and agonists or antagonists of	impaned wound iteating, and injection (e.g., injectious diseases and disorders as described in the "Infectious"
				the invention) include assays disclosed in	Diseases" section below, especially of the urinary tract and
				Xiong, S., et al., Proc Natl Acad Sci	skin), carpal tunnel syndrome and Dupuytren's
				U.S.A., 97(8):3948-53 (2000); Roder, K.,	contracture). An additional highly preferred
				et al., Eur J Biochem, 260(3):743-51	indication is obesity and/or complications associated with
				(1999); Oskouian B, et al., Biochem J, 317	obesity. Additional highly preferred indications include
•				(Pt 1):257-65 (1996); Berger, et al., Gene	weight loss or alternatively, weight gain. Aditional
				66:1-10 (1988); and, Cullen, B., et al.,	highly preferred indications are complications associated
				Methods in Enzymol. 216:362-368 (1992),	with insulin resistance.
				the contents of each of which is herein	
				incorporated by reference in its entirety.	
				Hepatocytes that may be used according to	
				these assays, such as H4IIE cells, are	
				publicly available (e.g., through the	
				ATCC) and/or may be routinely generated.	
				Exemplary hepatocytes that may be used	
				according to these assays include rat liver	
				hepatoma cell line(s) inducible with	
				glucocorticoids, insulin, or cAMP	
+				derivatives.	
145 H	HEBDF77	629	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies

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			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
			invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
-			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
-			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
			the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
			may be used according to these assays	pre-neoplastic conditions, such as, for example,
			include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
			2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
			with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma,
				Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, neutropenia,
-				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
		-		meningitis, Lyme Disease, cardiac reperfusion injury, and
-				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
				under "Infectious Disease").
146 HEBDQ91	099	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications

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include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include benign dysproliferative disorders and indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a
the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
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the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
transcription through the CD28 response	A highly preferred embodiment of the invention includes a
element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
modified to test CD28-response element	An alternative highly preferred embodiment of the
 activity of polypeptides of the invention	invention includes a method for inhibiting (e.g., reducing)
(including antibodies and agonists or	IL-2 production. Additional highly preferred
antagonists of the invention) include	indications include inflammation and inflammatory
assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
 Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. Highly
 (1997); Parra et al., J Immunol	preferred indications include neoplastic diseases (e.g.,
166(4):2437-2443 (2001); and Butscher et	melanoma, renal cell carcinoma, leukemia, lymphoma,
al., J Biol Chem 3(1):552-560 (1998), the	and/or as described below under "Hyperproliferative
contents of each of which are herein	Disorders"). Highly preferred indications include
 incorporated by reference in its entirety. T	neoplasms and cancers, such as, for example, melanoma
cells that may be used according to these	(e.g., metastatic melanoma), renal cell carcinoma (e.g.,
assays are publicly available (e.g., through	metastatic renal cell carcinoma), leukemia, lymphoma
the ATCC). Exemplary human T cells that	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
may be used according to these assays	pancreatic, esophageal, stomach, brain, liver and urinary
 include the SUPT cell line, which is a	cancer. Other preferred indications include benign
suspension culture of IL-2 and IL-4	dysproliferative disorders and pre-neoplastic conditions,
responsive T cells.	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. A highly preferred indication includes
	infection (e.g., AIDS, tuberculosis, infections associated
	with granulomatous disease, and osteoporosis, and/or as
	described below under "Infectious Disease"). A highly
	preferred indication is AIDS. Additional highly preferred
	indications include suppression of immune reactions to
	transplanted organs and/or tissues, uveitis, psoriasis, and
	tropical spastic paraparesis. Preferred indications
	include blood disorders (e.g., as described below under
•	"Immune Activity", "Blood-Related Disorders", and/or

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				"Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allerey.
147 HEBFR46	661	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic retinopathy, diabetes as described in the "Renal Disorders" section below), diabetic neuropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious bliseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated highly preferred indications are complications associated with highly preferred indications are complications associated

 661	Activation of transcription through AP1 response element in immune cells (such as T-cells).	according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167. Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element activity of polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997);	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications follow under "Hyperproliferative Disorders"). Highly preferred indications and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions,
		Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein	such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic

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	,	Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspensionculture cell line.	Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
147 HEBFR46 661	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma, leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon,

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				include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and alleroy.
147	HEBFR46	661	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under

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			invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
			agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
•			include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
-			Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
			Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
			Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
			85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
			Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
			(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
			Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
			al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
			and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
			268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
			by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
			may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
			publicly available (e.g., through the	allergy.
			ATCC). Exemplary human T cells that	
			may be used according to these assays	
			include the SUPT cell line, which is a	
			suspension culture of IL-2 and IL-4	
			responsive T cells.	
147 HEBFR46	199	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
		transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
		STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
		element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
•		cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
-			assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
			invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
			agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
-			regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
			modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
			Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
-			the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
			used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
			response element activity of the	below under "Hyperproliferative Disorders"). Preferred
			polypeptides of the invention (including	indications include neoplasms and cancers, such as,

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leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal,
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antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
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				Methods in Enzymol 216:362-368 (1992);	stomach, brain, liver and urinary cancer. Other preferred
				Henthorn et al., Proc Natl Acad Sci USA	indications include benign dysproliferative disorders and
				85:6342-6346 (1988); Black et al., Virus	pre-neoplastic conditions, such as, for example,
				Gnes 15(2):105-117 (1997); and Fraser et	hyperplasia, metaplasia, and/or dysplasia. Preferred
				al., 29(3):838-844 (1999), the contents of	indications also include anemia, pancytopenia, leukopenia,
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
		•		ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
				may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
				include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs,
				suspension culture of IL-2 and IL-4	asthma and allergy.
				responsive T cells.	
148	HEBGE07	799	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic

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			Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
			4587 (1995), the contents of each of which	and/or an infectious disease as described below under
			are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
			entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
			may be used according to these assays are	include anemia, pancytopenia, leukopenia,
			publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
			ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
			used according to these assays include the	granulomatous disease, inflammatory bowel disease,
		-	CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
			cells.	hemophilia, hypercoagulation, diabetes mellitus,
				endocarditis, meningitis, Lyme Disease, and asthma and allergy.
148 HEBGE07	662	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
		secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
		pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
			of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
			antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
			pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
			glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
			proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
			key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
			assays that may be used or routinely	stroke, and other diseases and disorders as described in the
			modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
			secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
			polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
			Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
			2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
			Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
			Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
			(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with

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			(1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology, 1007-130-167	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
149 HEGAUIS	663	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology,	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious

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Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by
	Production of IL-6
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				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
151	HELBU54	999	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune

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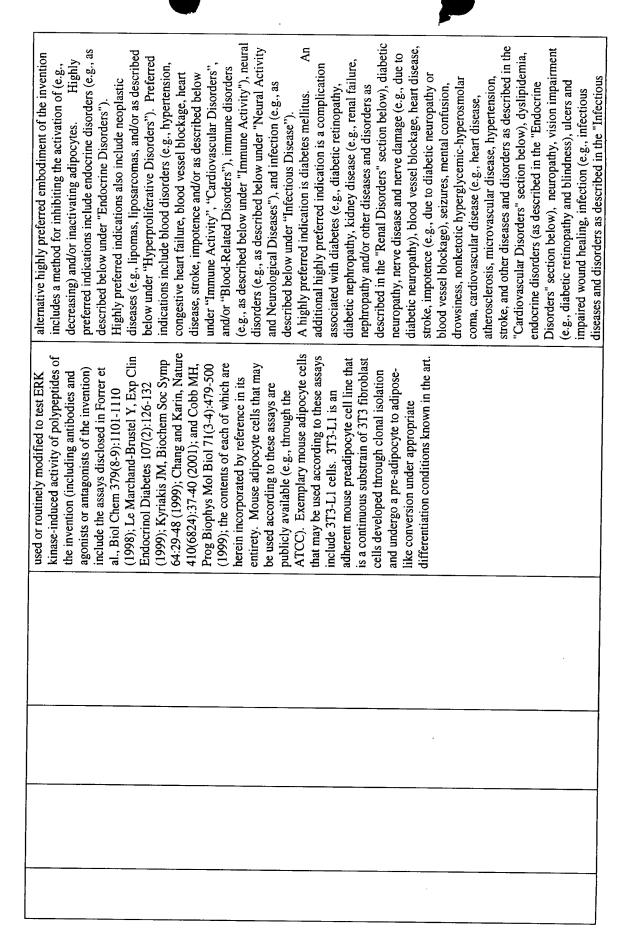
		in immune cells (such	routinely modified to assess the ability of	Activity" "Cardiovascular Disorders" and/or "Blood-
		as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
			antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
			the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
			other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
			transcription through the AP1 response	multiple sclerosis and/or as described below) and
			element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
			modified to test AP1-response element	highly preferred indications include inflammation and
			activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
-			(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
			antagonists of the invention) include	lymphoma, and/or as described below under
			assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
			66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
			Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
			Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
			Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
			4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
			Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
			cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
			assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
			the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
			may be used according to these assays	meningitis, and Lyme Disease.
			include the CTLL cell line, which is an IL-	
			2 dependent suspension-culture cell line	
\dashv			with cytotoxic activity.	
152 HELGG84	999	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		Det	all Lin-1 Milase assay, for Enn signal	includes a internol for stimulating adipocyte profileration.
		Fainway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			or differentiation are well known in the art	nge
			and may be used or routinely modified to	proliteration. A highly preferred embodiment of the
			assess the ability of polypeptides of the	invention includes a method for summating adipocyte
			invention (including antibodies and	differentiation. An affective figury preferred
			महत्तात्रत ज बातिहर्णात्रत ज बार गार्थात्राणा) त	כוווססתיווכוור סו נוול פוונוסוו וווכומתכט א וווכנווסת זסו

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promote or inhibit cell proliferation.	inhibiting adipocyte differentiation. A highly
activation, and differentiation. Exemplary	ion ir
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
 used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
 Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus.
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
 differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment

	,
(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders. Freferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for simulating (e.g., increasing) adipocyte activation. An
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	Activation of Adipocyte ERK Signaling Pathway
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Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones
	Production of IL-6
	899
	HEMBY47
	154

inflammatory disorders. Preferred indications	response element are well-known in the art	element in immune			
highly preferred indication is asuma. Highly preferred indications include inflammation and	Activators of Transcription (STAT6)	STAT6 response			
A highly preferred indication is allergy. Another	through the Signal Transducers and	transcription through			
	proliferation and functional activities.	Activation of	699	HEOMC46	155
	cytokines, initiate and upregulate T cell				
	which, when activated by antigen and/or				
	presenting cells in suspension culture,				
	art. Human dendritic cells are antigen				
described below under "Infectious Disease").	disclosed herein or otherwise known in the				
	assays may be isolated using techniques				<u>.</u>
meningitis, and Lyme Disease. An additional preferred	cells that may be used according to these				
hypercoagulation, diabetes mellitus, endocarditis	reference in its entirety. Human dendritic				
transplanted organs and tissues. hemonhilia	each of which are herein incorporated by				
neutrophilia nsoriasis sunnression of immine reactions to	158:2919-2925 (1997), the contents of				
lymphoma, arthritis, AIDS, granulomatous disease,	a practical approach Chapter 0:138-160				
lymphocytic anemia (ALL), multiple myeloma, Burkitt's	204(1999); Rowland et al., "Lymphocytes:				
leukopenia, thrombocytopenia, Hodgkin's disease, acute	J Biomolecular Screening 4:193-				
Preferred indications include anemia, pancytopenia	include assays disclosed in Miraglia et al.,				
example, hyperplasia, metaplasia, and/or dysplasia	agonists or antagonists of the invention)			,	
disorders and pre-neonlastic conditions such as for	the invention (including antibodies and				
Other preferred indications include benign dysproliferative	diffferentiation activity of polypeptides of				
esophageal, stomach, brain liver and prinary cancer	modified to test immunomodulatory and				
melanoma and proceeds broom live and	Such assays that may be used or routinely				
as myeloma plasmacytoma lenkemia tumphoma	proliferation and functional activities.		-		
preferred indications include accompany). Highly	the stimulation and upregulation of T cell				
helow under "Hymeraroliferative Discutation", II. 21.	production of cytokines, such as II6, and				
leoplastic diseases (e.g., myeloma, plasmacytoma,	immunomodulatory proteins evaluate the				
asthma and allergy. Highly preferred indications include	modulate I cell proliferation and function.				
disorders. Additional highly preferred indications include	immunomodulation and differentiation and				
indications include inflammation and inflammatory	the invention) to mediate				
B cell-mediated immune response. Highly preferred	antibodies and agonists or antagonists of	-			
	of polypeptides of the invention (including				
nreferred indications also include because I and	or routinely modified to assess the ability				
	Land though in the art and minut llaw are				

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include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below).	leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. Additional preferred indications include infectious disease as described below under "Infectious Disease").	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases").
and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through	the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen	and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Assays for the activation of transcription through the API response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of
cells (such as natural killer cells).			Activation of transcription through AP1 response element in immune cells (such as T-cells).
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			HEPBA14
			156

				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
			-	other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
		o)		assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
			-	Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
			£ - 1-1-2-2	Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
		-		4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
			•	may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
		·		2 dependent suspension-culture cell line	
ļ				with cytotoxic activity.	
157	HEQAH80	671	Activation of Natural	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		*******	Killer Cell ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating natural killer cell
			Signaling Pathway.	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting natural
				and may be used or routinely modified to	killer cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating natural killer cell differentiation. An
				agonists or antagonists of the invention) to	alternative highly preferred embodiment of the invention
				promote or inhibit cell proliferation,	includes a method for inhibiting natural killer cell
				activation, and differentiation. Exemplary	differentiation. Highly preferred indications include
				assays for ERK kinase activity that may be	neoplastic diseases (e.g., as described below under

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				used or routinely modified to test FRK	"Hynernroliferative Disorders") blood disorders (e.g. se
				kinase-induced activity of polypeptides of	described below under "Immune Activity",
				the invention (including antibodies and	"Cardiovascular Disorders", and/or "Blood-Related
				agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
		-		include the assays disclosed in Forrer et	, as
				al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
				(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
				64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
				410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
				Prog Biophys Mol Biol /1(3-4):4/9-500	preferred indications include autoimmune diseases (e.g.,
				(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
				neiem medipolated by reference mins	multiple scienosis and/or as described below) and
				entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
- 0				used according to these assays are publicly	highly preferred indications include inflammation and
				available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
				Exemplary natural killer cells that may be	also include cancers such as, kidney, melanoma, prostate,
				used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
				human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.
				example, NK-YT cells which have	Other preferred indications include benign dysproliferative
				cytolytic and cytotoxic activity) or primary	disorders and pre-neoplastic conditions, such as, for
				NK cells.	example, hyperplasia, metaplasia, and/or dysplasia.
					Other highly preferred indications include, pancytopenia,
					leukopenia, leukemias, Hodgkin's disease, acute
					lymphocytic anemia (ALL), arthritis, asthma, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, psoriasis, immune reactions to transplanted organs
					and tissues, endocarditis, meningitis, Lyme Disease, and
150	UEODESO	063	3	.100 1 2111	allergies.
	EQDF09	7/0	Activation of	Kinase assay. JINK and p38 kinase assays	A highly preferred embodiment of the invention
			Endothelial Cell p38 or	tor signal transduction that regulate cell	includes a method for stimulating endothelial cell growth.
			JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the
,			Pathway.	well known in the art and may be used or	invention includes a method for inhibiting endothelial cell
				routinely modified to assess the ability of	growth. A highly preferred embodiment of the
				polypeptides of the invention (including	invention includes a method for stimulating endothelial
				antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred
				the invention) to promote or inhibit cell	embodiment of the invention includes a method for
				proliferation, activation, and apoptosis.	inhibiting endothelial cell proliferation. A highly

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	Exemplary assays for JNK and p38 kinase	preferred embodiment of the invention includes a method
	activity that may be used or routinely	tor stimulating apoptosis of endothelial cells. An
	modified to test JNK and p38 kinase-	alternative highly preferred embodiment of the invention
-	induced activity of polypeptides of the	(e)
	invention (including antibodies and	apoptosis of endothelial cells. A highly preferred
	agonists or antagonists of the invention)	embodiment of the invention includes a method for
	include the assays disclosed in Forrer et	stimulating (e.g., increasing) endothelial cell activation.
	al., Biol Chem 379(8-9):1101-1110	An alternative highly preferred embodiment of the
	(1998); Gupta et al., Exp Cell Res 247(2):	invention includes a method for inhibiting (e.g.,
	495-504 (1999); Kyriakis JM, Biochem	decreasing) the activation of and/or inactivating
	Soc Symp 64:29-48 (1999); Chang and	endothelial cells. A highly preferred embodiment of
	Karin, Nature 410(6824):37-40 (2001);	the invention includes a method for stimulating
-	and Cobb MH, Prog Biophys Mol Biol	angiogenisis. An alternative highly preferred embodiment
	71(3-4):479-500 (1999); the contents of	of the invention includes a method for inhibiting
	each of which are herein incorporated by	angiogenesis. A highly preferred embodiment of the
	reference in its entirety. Endothelial cells	invention includes a method for reducing cardiac
	that may be used according to these assays	hypertrophy. An alternative highly preferred embodiment
	are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
	ATCC). Exemplary endothelial cells that	hypertrophy. Highly preferred indications include
	may be used according to these assays	neoplastic diseases (e.g., as described below under
	include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the
	cells (HUVEC), which are endothelial	cardiovascular system (e.g., heart disease, congestive heart
	cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyopathy,
	are involved in functions that include, but	valvular regurgitation, left ventricular dysfunction,
	are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease,
	permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
	cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
		overload, and/or as described below under
		"Cardiovascular Disorders"). Highly preferred indications
		include cardiovascular, endothelial and/or angiogenic
		disorders (e.g., systemic disorders that affect vessels such
		as diabetes mellitus, as well as diseases of the vessels
		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred

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				"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
159 HETCI16	6 673	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine Disorders (e.g., as described below under "Endocrine Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), and infection (e.g., as
			publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells	described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An

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that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	ndicat
	or alternatively, weight gain. Additional highly
	ns are
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	hies,
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and
	breast, colon, and kidney cancer. Additional preferred
	indications include melanoma, prostate, lung, pancreatic,
	esophageal, stomach, brain, liver, and urinary cancer.

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Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred embodiment of mucosal indication is the stimulation or enhancement of mucosal indication is the stimulation or enhancement of mucosal indication is the stimulation or enhancement of mucosal indication; Highly preferred indications include blood disorders (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-mediated immune response. Highly preferred indications include asthma and allergy. Highly preferred indications include asthma and allergy. Highly preferred indications include neoplasms and cancers, such as myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate modulate T cell proliferation and functional activities. Such assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraplia et al.
	Production of IL-6
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				J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
160	HETDW58	674	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transal anted organs

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				antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
161	HETEY67	675	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity," "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred

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			the invention) to mediate	indications include inflammation and infla
			immunomodulation and differentiation and	disorders Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
			diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
			the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
			agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
			include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
			J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
			a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease.
			(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia.
			158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
			each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
			reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
			cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
			assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
			disclosed herein or otherwise known in the	described below under "Infectious Disease").
			art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
-			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
2011 C71			proliferation and functional activities.	
	٥	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
		transcription inrough	through the cAMP response element are	described below under "Immune Activity", "Blood-
		cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
		element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
-		cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
	_		antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
			the invention) to increase cAMP, bind to	arthritis, systemic lupus erythematosis, multiple sclerosis
			CREB transcription factor, and modulate	and/or as described below), immunodeficiencies (e.g., as

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			expression of genes involved in a wide	described below), boosting a T cell-mediated immune
			variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
			assays for transcription through the cAMP	response. Additional preferred indications include
•			response element that may be used or	inflammation and inflammatory disorders. Highly
			routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
			element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
			invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
			agonists or antagonists of the invention)	indications include neoplasms and cancers, such as,
			include assays disclosed in Berger et al.,	leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's
			Gene 66:1-10 (1998); Cullen and Malm,	lymphoma, non-Hodgkins lymphoma, Hodgkin's disease),
			Methods in Enzymol 216:362-368 (1992);	melanoma, and prostate, breast, lung, colon, pancreatic,
		•	Henthorn et al., Proc Natl Acad Sci USA	esophageal, stomach, brain, liver and urinary cancer.
			85:6342-6346 (1988); Black et al., Virus	Other preferred indications include benign dysproliferative
			Genes 15(2):105-117 (1997); and	disorders and pre-neoplastic conditions, such as, for
			Belkowski et al., J Immunol 161(2):659-	example, hyperplasia, metaplasia, and/or dysplasia.
			665 (1998), the contents of each of which	Preferred indications include anemia, pancytopenia,
			are herein incorporated by reference in its	leukopenia, thrombocytopenia, acute lymphocytic anemia
			entirety. T cells that may be used	(ALL), plasmacytomas, multiple myeloma, arthritis,
			according to these assays are publicly	AIDS, granulomatous disease, inflammatory bowel
			available (e.g., through the ATCC).	disease, sepsis, neutropenia, neutrophilia, psoriasis,
			Exemplary human T cells that may be used	suppression of immune reactions to transplanted organs
			according to these assays include the	and tissues, hemophilia, hypercoagulation, diabetes
			JURKAT cell line, which is a suspension	mellitus, endocarditis, meningitis, Lyme Disease, and
			culture of leukemia cells that produce IL-2	asthma and allergy.
+			when stimulated.	
162 HFCDW95	929	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
		transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
		NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
		element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
		cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
			antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
			the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
			transcription factors and modulate	described below), and immunodeficiencies (e.g., as
			expression of immunomodulatory genes.	described below). An additional highly preferred
			Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
			the NFKB response element that may be	disease as described below under "Infectious Disease").
			used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases

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				response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	(e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, ALDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune
163	HFCE104	677	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to	A highly preferred indication is diabetes mellitus. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious

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polypeptides of the invention (including antibodies and agoniss or antagonists of antibodies and agonists of antagonists of antibodies and agonists of antagonists of all antagonic antibodies. J. 18iol Chem., 273(21):1428-22 (1989); Mora. S., et al., J. 18iol Chem., 275(21):16323-8 (2000), Liu, M.L., et al., J. 18iol Chem., 265(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in trangenic mice", J. 18iol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 18iol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 18iol Chem. 2001 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 18iol Chem. 2001 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 18iol Chem. 2001 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 18iol Chem. 2001 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 18iol Chem. 2001 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and CLUT4 promoter in trangenic mice", J. 19iol Chem. 2001 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and Aug 4;275(31):23666-73; and Au					(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
antibodies and agonists or antagonists of antibodies and agonists of antibodies and agonists or antagonists of the invention) include assays disclosed in Thai, M.V., et al., J Biol Chem. 20(45):28514-21 (1998); Mora, S., et al., J Biol Chem. 20(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be toutinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be toutinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell line which is an adherent mouse preadipocyte cells that may be such according to these assays include the mouse 373-L1 cell are a continuous substrain of 373 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelife continuous substrain of 373 fibroblasts and continuous substrain of 373 fibroblasts and the strong effects on B cells. L-6 participates in IL-6 participated in Il-6 participated in Il-6 participated in Il-6 participated in Il-6 p					polypeptides of the invention (including	skin), carpal tunnel syndrome and Dupuytren's
in the invention) include assays disclosed in the invention) include assays disclosed in the invention) include assays disclosed in the invention of ILO Chem. 273(23):1428-5-9 (1998); Mora. S., et al., J Biol Chem. 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug. 4:275(31):2366-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen. B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirely. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 713-L1 cells are a continuous substrain of 313 fibroblasts developed through clonal isolation. These assays include the mouse 713-L1 cells are a continuous autorinary and isolation. These are according to the according t					antibodies and agonists or antagonists of	contracture). An additional highly preferred
inThai, M.V., et al., J Biol Chem, 273(21):1428-29 (1998); Mora, S., et al., J Biol Chem, 275(21):1632-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):2814-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem, 2000 Aug 4275(31):2366-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymont. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell line which is an adherent mouse preadipocyte cells undergo a pre-adipocyte to adiposecills en merces and pre-adipocyte to adiposecills en merces in the production and has strong effects on B cells. L.6 participates in IL.4 induced lgE production and near strong effects on B cells. L.6 participates in IL.4 induced lgE production and near strong effects on B cells. L.6 participates in IL.4 induced lgE production and near strong effects on B cells. L.6 participates in IL.4 induced lgE production and near strong effects on B cells. L.6 participates in IL.4 induced lgE production and near strong effects on B cells. L.6 participates in IL.4 induced lgE production and increases lgA oproducion lgAp plays a proble in microas inmunity.) II.6 induced lgE production and increases lgAp aproducion and increases lgAp aproducion and increases lgAp aproducion and increases lgAp aproducion and and an approach and and an approach and and an approach and and an approach and a					the invention) include assays disclosed	indication is obesity and/or complications associated with
273(23):14285-92 (1998); Mora, S., et al., 1 Biol Chem, 275(21):1632-8 (2000); Liu, M.L., et al., 1 Biol Chem, 269(45):28514- 21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem, 2000 Aug 4:275(31):23666- 73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) andor may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell sine which is an adherent mouse preadipocyte cell line. Mouse 373-L1 cells are a continuous substrain of 373 fbroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose- like conversion under appropriate differentiation culture conditions. HFCFD04 678 Production of IL-6 participates in IL-4 induced lgE production and increases lgA production (184 plays a role in muroseal immunity). If 6 induced					inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
HECEDO4 678 (2000); Liu, ML., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, ML., et al., J Biol Chem, 206(45):28514- 21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4:275(31):23666- 73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse preadipocyte cells that may be used according to these assays include the mouse preadipocyte cells that may be used according to these assays include the mouse preadipocyte cell line which is an adherent mouse preadipocyte of cell line which is an adherent mouse preadipocyte to adiposelike conversion under appropriate differentiation culture conditions. HFCEDO4 678 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and in in mucosal in municosal in munico				•	273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
M.L., et al., J Biol Chem, 269(45):28514– 21 (1994), "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human CLU74 promoter in transgenic mice.", J Biol Chem. 2000 Aug 4;275(31):23666–73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herin incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 9713-L1 cell ine which is an adherent mouse preadipocyte to adipocyte cell line. Mouse 373-L1 cells are a continuous substrain of 373 fbroblasts developed through clond isolation. These cells undergo a pre-adipocyte to adipocyte pre-adipocyte or adipocyte cells and has strong effects on B cells. L-6 participates in L-4 induced lgE production and interesses leaved in municos. III-6 in murcosal information (184 plays a coll information (184 plays a coll information (186 plays a c					J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 5T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions. HFCFD04 678 Production of IL-6 EMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in microsel immunity) II-6 induced					M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666- 73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fbroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose- like conversion under appropriate differentiation culture conditions. IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and in micreases IgA production (IgA plays a role in micreases IgA production (IgA plays a					21 (1994); "Identification of a 30-base pair	
binding protein that regulates the human GLUT4 promoter in transgenic mice", J BIOI Chem. 2000 Aug 4;275(31):23666-73; Briger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell line which is an adherent mouse preadipocyte cells that may be used according to these assays include the mouse 373-L1 cells are a continuous substrain of 373 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions. HFCFD04 678 Production of IL-6 IRMAT. IL-6 is produced by T cells and has strong effects on B cells. L1-6 participates in IL-4 induced 1gE production and increases 1gA production (IgA plays a role in murocal immunity) II-6 induces					regulatory element and novel DNA	
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Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HFCFD04 678 Production of IL-6 In-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in murosal immunity) II-6 induced					GLUT4 promoter in transgenic mice", J	
73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose- like conversion under appropriate differentiation culture conditions. HFCFD04 678 Production of IL-6 participates in IL-4 induced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in munosal immunity) IL-6 induces	•				Biol Chem. 2000 Aug 4;275(31):23666-	
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HFCFD04 678 Production of IL-6 FMAT. IL-6 is production and increases IgA production (IgA plays a role in mucosal immunity) IL-6 induces					developed through clonal isolation. These	
HFCFD04 678 Production of IL-6 IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity) IL-6 induces					cells undergo a pre-adipocyte to adipose-	
HFCFD04 678 Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces					like conversion under appropriate	
HrCrD04 678 Production of IL-6 IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity) II-6 induces	╁		ļ		differentiation culture conditions.	
o n		FD04	8/9		L-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
о п а					and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
					participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
reducing) II -6 production					and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
I reducing) in a production.					role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred

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	cytotoxic T cells. Deregulated expression	on indication is the stimulation or enhancement of mucosal	
	of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood	
	disease, plasmacytomas, myelomas, and	disorders (e	
	chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or	
	Assays for immunomodulatory and		
	differentiation factor proteins produced by		
	a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,	
	expression level is strongly regulated by	-	_
	cytokines, growth factors, and hormones		
	are well known in the art and may be used		
	or routinely modified to assess the ability		
	of polypeptides of the invention (including		_
	antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred	
	the invention) to mediate		
	immunomodulation and differentiation and		
	modulate T cell proliferation and function.		_
	Exemplary assays that test for		
	immunomodulatory proteins evaluate the		
	production of cytokines, such as IL-6, and		
	the stimulation and upregulation of T cell	_	
	proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,	
	Such assays that may be used or routinely	ly melanoma, and prostate, breast, lung, colon, pancreatic,	
	modified to test immunomodulatory and		
	diffferentiation activity of polypeptides of	of Other preferred indications include benign dysproliferative	
	the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for	
4 11	agonists or antagonists of the invention)		
	include assays disclosed in Miraglia et al.,		
	J Biomolecular Screening 4:193-		
	204(1999); Rowland et al., "Lymphocytes:		
	a practical approach" Chapter 6:138-160		
	(2000); and Verhasselt et al., J Immunol		
	158:2919-2925 (1997), the contents of		
	each of which are herein incorporated by		
	reference in its entirety. Human dendritic	ic hypercoagulation, diabetes mellitus, endocarditis,	
	cells that may be used according to these	•	
	assays may be isolated using techniques	indication is infection (e.g., an infectious disease as	
	disclosed herein or otherwise known in the	\dashv	

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				art Human dendritic cells are antigen	
-				presenting cells in suspension culture.	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
165	HFCFE20	629	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			PI3 Kinase Signalling	an GSK-3 assays, for PI3 kinase signal	includes a method for increasing adipocyte survival An
			Pathway	transduction that regulate glucose	alternative highly preferred embodiment of the invention
	•			metabolism and cell survival are well-	includes a method for decreasing adipocyte survival. A
				known in the art and may be used or	preferred embodiment of the invention includes a method
				routinely modified to assess the ability of	for stimulating adipocyte proliferation. An alternative
				polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for inhibiting adipocyte proliferation. A
				the invention) to promote or inhibit	preferred embodiment of the invention includes a method
				glucose metabolism and cell survival.	for stimulating adipocyte differentiation. An alternative
				Exemplary assays for PI3 kinase activity	highly preferred embodiment of the invention includes a
				that may be used or routinely modified to	method for inhibiting adipocyte differentiation. Highly
				test PI3 kinase-induced activity of	preferred indications include endocrine disorders (e.g., as
				polypeptides of the invention (including	described below under "Endocrine Disorders").
				antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
				the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
				Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
				1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
				49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
				Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
				contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
				incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
				Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
				according to these assays are publicly	described below under "Neural Activity and Neurological
				available (e.g., through the ATCC).	on (e.§
				Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication
				be used according to these assays include	is diabetes mellitus. An additional highly preferred
				3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
				mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
				continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
				developed through clonal isolation and	disorders as described in the "Renal Disorders" section
				undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve

	differentiation conditions known in the art.	
		diabetic neuropathy or blood vessel blockage), seizures,
		mental confusion, drowsiness, nonketotic hyperglycemic-
		hyperosmolar coma, cardiovascular disease (e.g., heart
		disease, atherosclerosis, microvascular disease,
		hypertension, stroke, and other diseases and disorders as
		described in the "Cardiovascular Disorders" section
		below), dyslipidemia, endocrine disorders (as described in
		the "Endocrine Disorders" section below), neuropathy,
		vision impairment (e.g., diabetic retinopathy and
		blindness), ulcers and impaired wound healing, infection
		(e.g., infectious diseases and disorders as described in the
		"Infectious Diseases" section below, especially of the
		urinary tract and skin), carpal tunnel syndrome and
		Dupuytren's contracture). An additional highly
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		associated with obesity. Additional highly preferred
		indications include weight loss or alternatively, weight
		gain. Additional highly preferred indications are
		lication
		Additional highly preferred indications are disorders of the
		musculoskeletal systems including myopathies, muscular
		dystrophy, and/or as described herein.
		Additional highly preferred indications include,
		hypertension, coronary artery disease, dyslipidemia,
		gallstones, osteoarthritis, degenerative arthritis, eating
		disorders, fibrosis, cachexia, and kidney diseases or
-		disorders. Highly preferred indications include
		neoplasms and cancer, such as, lipoma, liposarcoma,
		Iymphoma, leukemia and breast, colon, and kidney cancer.
		Additional highly preferred indications include melanoma,
		prostate, lung, pancreatic, esophageal, stomach, brain,
		liver, and urinary cancer. Other preferred indications
		include benign dysproliferative disorders and pre-
		neoplastic conditions, such as, for example, hyperplasia,
		metaplasia, and/or dysplasia.

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A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for	inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred	embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease.	hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that
Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in	endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126	(2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include boxing cortic and others assays include boxing cortic and others.	(bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.
Endothelial Cell Apoptosis			
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	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,
	coronary artery disease, inflammatory vasculitides,
	Reynaud's disease and Reynaud's phenomenom,
	aneurysms, restenosis; venous and lymphatic disorders
	such as thrombophlebitis, lymphangitis, and lymphedema;
	and other vascular disorders such as peripheral vascular
	disease, and cancer. Highly preferred indications also
	include trauma such as wounds, burns, and injured tissue
	(e.g., vascular injury such as, injury resulting from balloon
	angioplasty, and atheroschlerotic lesions), implant
	fixation, scarring, ischemia reperfusion injury, rheumatoid
	arthritis, cerebrovascular disease, renal diseases such as
	acute renal failure, and osteoporosis. Additional highly
	preferred indications include stroke, graft rejection,
	diabetic or other retinopathies, thrombotic and coagulative
	disorders, vascularitis, lymph angiogenesis, sexual
	disorders, age-related macular degeneration, and treatment
	/prevention of endometriosis and related conditions.
	Additional highly preferred indications include fibromas,
	heart disease, cardiac arrest, heart valve disease, and

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					month or director Descharation distributed blood
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				4	disolucis (e.g., as described below under minimie Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
166	HFEAY59	089		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
			****	macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
				invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
				agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
				mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
				inflammatory activities, modulate TH2	indications include inflammation and inflammatory
				helper cell function, and/or mediate	disorders. Additional preferred indications include
				humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
				Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
				immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
				production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
				gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,

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brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or artagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., Tymphocytes: a practical approach." Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol,
	Production of ICAM-1
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167 HFGAJ16	189	Production of MIP1alpha	156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC). MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., 1 Biomolecular Screening 4:193-	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and
			204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et	allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such

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Production of TNF TNFa FMAT. Assays for alpha by T cells immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, alpha production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) TNF alpha production. Cytotoxic effects on a variety of rinflammatory and exercised below under "Immune Activity", "Blood-routinely modified to assess the ability of Related Disorders", and/or "Cardiovascular Disorders"), polypeptides of the invention (including invention) to mediate invention) to mediate manomodulation, modulate immunity. Exemplary assays that test for immunomodulatory proteins evaluate the immunomodulatory proteins evaluate the referred indication include and cancers and additional highly preferred indications include autoimmune response, and mecrosis factor alpha (TNFa), and the may be used or routinely modified to test.
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				antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol	malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas,
				160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated	multiple myeloma, Burkitt's lymphoma, arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An
				using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors	additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
169	HFIJA29	683	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes allergy. A highly preferred
				of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated	atic rre uke bed

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immunonodulatory profesis evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention include the assays disclosed in Miragila et al., 1 Biomolecular Screening 4.193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzaler at al., J Clin. Lab Anal 8(5):277-283 (11994); Yssel et al., Res Immunol 1(3):257-261 (2000); Gonzaler at al., J Clin. Lab Anal 8(5):277-283 (11994); Yssel et al., Res Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirey. Human T cells that may be used according to these assays and ceptress at T cell receptor and CD3, CD4, or CD9. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. 169 HFIJA29 683 Ubregulation of CD132 FMAT. CD152 (a.k.a. CTLA-4) and activation of T cells profiferation. Reduced CD152 expression			imminity Exemplary assays that feet for	include neonlasms and cancers such as for example
HFIJA29 683 Upregulation of CD152 and activation of T cells	-		imminus and international and international	Testing in the state of the sta
HFIJA29 683 Upregulation of CD152 and activation of T cells			initionicontactory proteins evaluate the	leukemia, iympnoma, melanoma, and prostate, oreast,
HFIJA29 683 Upregulation of CD152 and activation of T cells			production of cytokines, such as IL-4, and	lung, colon, pancreatic, esophageal, stomach, brain, liver
HFIJA29 683 Upregulation of CD152 and activation of T cells			the stimulation of immune cells, such as B	and urinary cancer. Other preferred indications include
HFIJA29 683 Upregulation of CD152 and activation of T cells			cells, T cells, macrophages and mast cells.	benign dysproliferative disorders and pre-neoplastic
HFIJA29 683 Upregulation of CD152 and activation of T cells			Such assays that may be used or routinely	conditions, such as, for example, hyperplasia, metaplasia,
HFIJA29 683 Upregulation of CD152 and activation of T cells			modified to test immunomodulatory	and/or dysplasia. Preferred indications include blood
HFIJA29 683 Upregulation of CD152 and activation of T cells		-	activity of polypeptides of the invention	disorders (e.g., as described below under "Immune
HFIJA29 683 Upregulation of CD152 and activation of T cells			(including antibodies and agonists or	Activity", "Blood-Related Disorders", and/or
HFIJA29 683 Upregulation of CD152 and activation of T cells	-		antagonists of the invention) include the	"Cardiovascular Disorders"). Preferred indications include
HFIJA29 683 Upregulation of CD152 and activation of T cells			assays disclosed in Miraglia et al., J	autoimmune diseases (e.g., rheumatoid arthritis, systemic
HFIJA29 683 Upregulation of CD152 and activation of T cells			Biomolecular Screening 4:193-204 (1999);	lupus erythematosis, multiple sclerosis and/or as described
HFIJA29 683 Upregulation of CD152 and activation of T cells			Rowland et al., "Lymphocytes: a practical	below) and immunodeficiencies (e.g., as described below).
HFIJA29 683 Upregulation of CD152 and activation of T cells			approach" Chapter 6:138-160 (2000);	Preferred indications include anemia, pancytopenia,
HFIJA29 683 Upregulation of CD152 and activation of T cells			Gonzalez et al., J Clin Lab Anal 8(5):277-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
HFIJA29 683 Upregulation of CD152 and activation of T cells			283 (1194); Yssel et al., Res Immunol	lymphocytic anemia (ALL), plasmacytomas, multiple
HFIJA29 683 Upregulation of CD152 and activation of T cells			144(8):610-616 (1993); Bagley et al., Nat	myeloma, Burkitt's lymphoma, arthritis, AIDS,
HFIJA29 683 Upregulation of CD152 and activation of T cells			Immunol 1(3):257-261 (2000); and van der	granulomatous disease, inflammatory bowel disease,
HFIJA29 683 Upregulation of CD152 and activation of T cells			Graaff et al., Rheumatology (Oxford)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
HFIJA29 683 Upregulation of CD152 and activation of T cells			38(3):214-220 (1999), the contents of each	immune reactions to transplanted organs and tissues,
HFIJA29 683 Upregulation of CD152 and activation of T cells			of which are herein incorporated by	hemophilia, hypercoagulation, diabetes mellitus,
HFIJA29 683 Upregulation of CD152 and activation of T cells			reference in its entirety. Human T cells	endocarditis, meningitis, and Lyme Disease. An
HFIJA29 683 Upregulation of CD152 and activation of T cells			that may be used according to these assays	additonal preferred indication is infection (e.g., an
HFIJA29 683 Upregulation of CD152 and activation of T cells			may be isolated using techniques disclosed	infectious disease as described below under "Infectious
HFIJA29 683 Upregulation of CD152 and activation of T cells			herein or otherwise known in the art.	Disease").
HFIJA29 683 Upregulation of CD152 and activation of T cells			Human T cells are primary human	
HFIJA29 683 Upregulation of CD152 and activation of T cells			lymphocytes that mature in the thymus and	
HFIJA29 683 Upregulation of CD152 and activation of T cells			express a T cell receptor and CD3, CD4, or	
HFIJA29 683 Upregulation of CD152 and activation of T cells			CD8. These cells mediate humoral or cell-	
HFIJA29 683 Upregulation of CD152 and activation of T cells			mediated immunity and may be	
HFIJA29 683 Upregulation of CD152 and activation of T cells			preactivated to enhance responsiveness to	
HFIJA29 683 Upregulation of CD152 and activation of T cells			immunomodulatory factors.	
T cells	HFIJA29	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression		and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
proliferation. Reduced CD152 expression			CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				method for inhibiting the activation of and/or inactivating
has been linked to hyperproliferative and			has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the

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	duloininune diseases. Overexpression of	invention includes a method for innibiting 1 cell
	CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
	immunoresponses. Assays for	.=
	immunomodulatory proteins important in	proliferation. Highly preferred indications include
	the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
	expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
	CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
	may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
	assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
	invention (including antibodies and	described below), immunodeficiencies (e.g., as described
	agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
	modulate the activation of T cells,	suppressing a T cell-mediated immune response.
	maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
	mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
	immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
	immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
	upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
	as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
	Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
	modified to test immunomodulatory	Other preferred indications include benign dysproliferative
	activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
	(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
	antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
	example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
	(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
	practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
	(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
	77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
	Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
	Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
	321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
	are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
	entirety. Human T cells that may be used	described below under "Infectious Disease").
	according to these assays may be isolated	
-	using techniques disclosed herein or	
	otherwise known in the art. Human T cells	

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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation. Vascular Disease.
are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	kinase assays nase family RK) are well s used or the ability of nn (including nagonists of r inhibit cell, and/or une cells such s for MAP may be used polypeptides in: Rincon M., 339-345 mmunol, akamoto H, et 5857-35862 of which are ence in its e cells (for be used	expression of vn in the art and sly modified to lypeptides of the
	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).	Production of ICAM-1
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	HFIJA68	HFKES05
	170	171

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			invention (including antibodies and	Athereosclerosis. Restenosis, and Stroke
			agonists or antagonists of the invention) to	
			regulate ICAM-1 expression. Exemplary	
			assays that may be used or routinely	
			modified to measure ICAM-1 expression	,
			include assays disclosed in: Takacs P, et al,	
			FASEB J, 15(2):279-281 (2001); and,	
			Miyamoto K, et al., Am J Pathol,	
			156(5):1733-1739 (2000), the contents of	
			each of which is herein incorporated by	
			reference in its entirety. Cells that may be	
			used according to these assays are publicly	
			available (e.g., through the ATCC) and/or	
			may be routinely generated. Exemplary	
			cells that may be used according to these	
			assays include microvascular endothelial	
-			cells (MVEC).	
172 HFKEU12	989	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
-			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
			growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
			transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
			invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,

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				Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease.")
173	HFPCZ55	687	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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				invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
174	HFPDR62	889	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly

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agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	sec
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.

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HFPDS07 68	689	Activation of Natural Killer Cell ERK Signaling Pathway.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of	Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, Iymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include meoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity".
			the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	"Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity") and infections (e.g., as described below under "Infectious Disease"). Preferred

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HFPDS07	689	Upregulation of HLA- DR and activation of T cells	(1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cells which have example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells. HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis). Assays for immunomodulatory moterns evenesed on MHC class II	indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below), hooting a Toell mediated immunose disease, and and immunodeficiencies (e.g., as described below), hooting a median munodeficiencies (e.g., as described below), and immunodeficiencies (e.g., as described below), and immunodeficiencies (e.g., as described below), and immunodeficiencies (e.g., as described below), and described immunodeficiencies (e.g., as described below), and described below).
			expressing T cells and antigen presenting cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate	alternatively, suppressing a T cell-mediated immune response. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section

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humoral or cell-mediated immunity. Evenulary account that for	below), diabetic neuropathy, nerve disease and nerve	
immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to	
upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,	
such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-	
activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart	
be used or routinely modified to test	disease, atherosclerosis, microvascular disease,	
immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as	
polypeptides of the invention (including	described in the "Cardiovascular Disorders" section	
antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in	
the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,	
assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and	
Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and	
Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as	
approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,	
Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel	
89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An	
Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or	
Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly	
117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,	
Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications	
the contents of each of which are herein	are complications associated with insulin resistance.	
incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the	
Human T cells that may be used according	musculoskeletal systems including myopathies, muscular	
to these assays may be isolated using	dystrophy, and/or as described herein.	
techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,	
 known in the art. Human T cells are	and/or as described below under "Infectious Disease").	
primary human lymphocytes that mature in	Preferred indications include endocrine disorders (e.g., as	
the thymus and express a T Cell receptor	described below under "Endocrine Disorders"), and	
and CD3, CD4, or CD8. These cells	neoplastic diseases (e.g., leukemia, lymphoma, and/or as	
mediate humoral or cell-mediated	described below under "Hyperproliferative Disorders").	
immunity and may be preactivated to	Preferred indications include neoplasms and cancer, such	
enhance responsiveness to	as, for example, leukemia, lymphoma, and prostate, breast,	
immunomodulatory factors.	lung, colon, pancreatic, esophageal, stomach, brain, liver	
	and urinary cancer. Other preferred indications include	
	benign dysproliferative disorders and pre-neoplastic	
	conditions, such as, for example, hyperplasia, metaplasia,	

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					and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and inflammatory disorders, and asthma and allergy.
176	HFRAB10	069	Production of MIP lalpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., I Biomolecular Screening 4:193-	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll	allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly

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				Surg Edno 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
·				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
•				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
177 HF	HFTBM38	691	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
		_		autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
		_		modulate the activation of T cells,	suppressing a T cell-mediated immune response.
		_		maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,

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			as CD152, and the activation of T cells.	melanoma and prostate breast lung colon pancreatic
			Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
	•••••		modified to test immunomodulatory	Other preferred indications include benign dysproliferative
			activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
			(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
			antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
			example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
			(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
			(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
			77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
			Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
			Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
			321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
			are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
			entirety. Human T cells that may be used	described below under "Infectious Disease").
			according to these assays may be isolated	
			using techniques disclosed herein or	
			otherwise known in the art. Human T cells	
			are primary human lymphocytes that	
			mature in the thymus and express a T Cell	
			receptor and CD3, CD4, or CD8. These	
			cells mediate humoral or cell-mediated	
			immunity and may be preactivated to	
			enhance responsiveness to	
\dashv			immunomodulatory factors.	
177 HFTBM38	691	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
-		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
		as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
			expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
			and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple

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				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
-				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
-				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
•				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
+				and the second s	under "Infectious Disease").
178	HFTDH56	692	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention
			Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
				may be used or routinely modified to	An alternative highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for inhibiting endothelial cell
			-, .	invention (including antibodies and	growth. A highly preferred embodiment of the
				agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
				promote caspase protease-mediated	cell proliferation. An alternative highly preferred

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	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,
	coronary artery disease, inflammatory vasculitides,
	Reynaud's disease and Reynaud's phenomenom,
	aneurysms, restenosis; venous and lymphatic disorders
	such as thrombophlebitis, lymphangitis, and lymphedema;
	and other vascular disorders such as peripheral vascular
	disease, and cancer. Highly preferred indications also
	(e.g., vascular injury such as, injury resulting from balloon
	angioplasty, and atheroschlerotic lesions), implant
	fixation, scarring, ischemia reperfusion injury, rheumatoid
	arthritis, cerebrovascular disease, renal diseases such as
	acute renal failure, and osteoporosis. Additional highly
	preferred indications include stroke, graft rejection,
	diabetic or other retinopathies, thrombotic and coagulative
	disorders, vascularitis, lymph angiogenesis, sexual
	disorders, age-related macular degeneration, and treatment
	/prevention of endometriosis and related conditions.
	Additional highly preferred indications include fibromas,
	heart disease, cardiac arrest, heart valve disease, and
	vascular disease. Preferred indications include blood
	disorders (e.g., as described below under "Immune
	Activity", "Blood-Related Disorders", and/or
	"Cardiovascular Disorders"). Preferred indications include
	autoimmune diseases (e.g., rheumatoid arthritis, systemic
	lupus erythematosis, multiple sclerosis and/or as described
	below) and immunodeficiencies (e.g., as described below).

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					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
179	HFVGK35	693	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
-				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
		· · · ·		chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute

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HFVGK35 693	Δ.	Production of MCP-1	a practical approach." Chapter 6:138-160 (2000); and Verhasselt et al., I Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assent	lymphocytic anemia (ALL), multiple mycloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficianina also include anemia, pancytopenia, leukopenia, thombocytopenia, thodalvia, diseases
			cens. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include	roogkin s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoamlation, diabetes.

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				assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	mellitus, endocarditis, meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
180	HFVHW43	694	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in:	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious

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			Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance.
181	HFXAV37	Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for Pl3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for Pl3 kinase activity that may be used or routinely modified to test Pl3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. An alternative highly preferred embodiment of the invention includes a

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	the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
	Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
	1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
	49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
	Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
	contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
	incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
	Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
	according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
	available (e.g., through the ATCC).	described below under "Immune Activity",
	Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
	used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
	cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
	line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
	thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus.
	multinucleated myotubes and striated	additional highly preferred indication is a complication
	fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
		diabetic nephropathy, kidney disease (e.g., renal failure,
- Secretary		nephropathy and/or other diseases and disorders as
		described in the "Renal Disorders" section below), diabetic
		neuropathy, nerve disease and nerve damage (e.g, due to
		diabetic neuropathy), blood vessel blockage, heart disease,
		stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infections (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below, especially of the urinary tract and
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		contracture). An additional highly preferred indication

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182	HFXBN86	969	Production of MIP1alpha	MIP-lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to	is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia. A highly preferred embodiment of the invention includes a method for stimulating (e.g., reducing) MIPla production. A highly preferred indication is infection (e.g., an infectious disease as described below under
				assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely	"Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple

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				modified to test immunomodulatory and	mveloma. Burkitt's lymphoma. arthritis. AIDS.
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
		•		agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
	•			a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukernia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
183	HFXBT66	269	Production of IL-2 and	IL-2 FMAT. IL-2 is the principal T cell	A highly preferred embodiment of the invention
			activation of T cells	factor that allows T cell expansion and	includes a method for stimulating IL-2 production. An
				differentiation into effector cells. Assays	alternative highly preferred embodiment of the invention
				for immunomodulatory proteins secreted	includes a method for inhibiting (e.g., reducing) IL-2
				by TH1 cells that promote T cell and NK	production. A highly preferred embodiment of the
				cell growth and differentiation are well	invention includes a method for stimulating T cell
				known in the art and may be used or	expansion. An alternative highly preferred embodiment of
				routinely modified to assess the ability of	the invention includes a method for inhibiting T cell
				polypeptides of the invention (including	expansion. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating T cell
				the invention) to mediate	differentiation. In a specific embodiment, this method
				immunomodulation, promote immune cell	stimulates T cell differentiation into effector cells. An
				growth and differentiation, and/or mediate	alternative highly preferred embodiment of the invention

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	humoral or cell-mediated immunity.	includes a method for inhibiting T cell differentiation. In a
	Exemplary assays that test for	specific embodiment, this method inhibits the
	immunomodulatory proteins evaluate the	differentiation of T cells into effector cells. Highly
	production of cytokines, such as IL-2, and	preferred indications include neoplastic diseases (e.g.,
	the activation of T cells. Such assays that	melanoma, renal cell carcinoma, leukemia, lymphoma,
	may be used or routinely modified to test	and/or as described below under "Hyperproliferative
	immunomodulatory activity of	Disorders"). Highly preferred indications include
	polypeptides of the invention (including	neoplasms, such as, for example, melanoma (e.g.,
	antibodies and agonists or antagonists of	metastatic melanoma), renal cell carcinoma (e.g.,
	the invention) include the assays disclosed	metastatic renal cell carcinoma), leukemia, lymphoma
	in Miraglia et al., J Biomolecular	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
	Screening 4:193-204 (1999); Rowland et	pancreatic, esophageal, stomach, brain, liver, ovarian, and
	al., "Lymphocytes: a practical approach"	urinary cancer. Other preferred indications include benign
	Chapter 6:138-160 (2000); Laduda et al.,	dysproliferative disorders and pre-neoplastic conditions,
	Immunology 94(4):496-502 (1998); and	such as, for example, hyperplasia, metaplasia, and/or
	Powell et al., Immunol Rev 165:287-300	dysplasia. A highly preferred indication is infection (e.g.,
	(1998), the contents of each of which are	an infectious disease as described below under "Infectious
	herein incorporated by reference in its	Disease"). A highly preferred indication is AIDS and HIV
	entirety. Human T cells that may be used	infection. Additional highly preferred indications include
	according to these assays may be isolated	suppression of immune reactions to transplanted organs
,	using techniques disclosed herein or	and/or tissues, uveitis, psoriasis, and tropical spastic
	otherwise known in the art. Human T cells	paraparesis. Preferred indications include blood
	are primary human lymphocytes that	disorders (e.g., as described below under "Immune
	mature in the thymus and express a T cell	Activity", "Blood-Related Disorders", and/or
	receptor and CD3, CD4, or CD8. These	"Cardiovascular Disorders"). Preferred indications include
	cells mediate humoral or cell-mediated	autoimmune diseases (e.g., rheumatoid arthritis, systemic
	immunity and may be preactivated to	lupus erythematosis, multiple sclerosis and/or as described
	enhance responsiveness to	below), immunodeficiencies (e.g., as described below),
	immunomodulatory factors.	organ and tissue transplant rejection. Additional
		preferred indications include inflammation and
		inflammatory disorders. Preferred indications include
		anemia, pancytopenia, leukopenia, thrombocytopenia,
		Hodgkin's disease, acute lymphocytic anemia (ALL),
		plasmacytomas, multiple myeloma, Burkitt's lymphoma,
		Non-Hodgkin's lymphoma, Kaposi's sarcoma arthritis,
		granulomatous disease, inflammatory bowel disease,
		Hepatitis (e.g. Hepatitis C), sepsis, neutropenia,

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					neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
184	HFXFZ46	869	Upregulation of HLA-DR and activation of T cells	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular
				been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis,	Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
				systemic lupus erythematosis, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II	lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below), boosting a T cell mediated immuna resource and
				expressing T cells and antigen presenting cells are well known in the art and may be	alternatively, suppressing a T cell-mediated immune response. A highly preferred indication is diabetes
				used or routinely modified to assess the ability of polymentides of the invention	mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g. diabetic
				(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
				antagonists of the invention) to modulate the activation of T cells, and/or mediate	renal tailure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section
				humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
				Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
				immunomodulatory proteins evaluate the unregulation of MHC class II products	blockage, heart disease, stroke, impotence (e.g., due to diahetic neuronathy or blood vessel blockage) seizures
				such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
				activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
				be used or routinely modified to test immunomodulatory activity of	disease, atherosclerosis, microvascular disease, hypertension stroke and other diseases and disorders as
				polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
				antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
				the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
		·		assays disclosed in Miragina et al., J Biomolecular Screening 4:193.204 (1999):	vision impairment (e.g., diabetic retinopathy and blindness) ulcers and impaired wound healing and
				Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
				approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
				Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
				89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
		- uti	₩	Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
				Gansoacher and Zier, Cell Immunol	complications associated with obesity. Additional highly

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preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. An additional preferred indication is infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Preferred indications include endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammaton and allergy.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
Histochem Cytochem 40(11):1675-1683, the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the API response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the API response
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
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	HGBER72
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			element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
			modified to test AP1-response element	highly preferred indications include inflammation and
			activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
			(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
			antagonists of the invention) include	lymphoma, and/or as described below under
			assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
			66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
			Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
			Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
			Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
			4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
			Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
			Mouse T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
-			to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
			through the ATCC). Exemplary mouse T	reactions to transplanted organs and tissues, endocarditis,
			cells that may be used according to these	meningitis, and Lyme Disease.
			assays include the HT2 cell line, which is	
			an IL-2 dependent suspension culture cell	
			line that also responds to IL-4.	
185 HGBER72	669	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
		transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
		NFAT response in	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
		immune cells (such as	known in the art and may be used or	Disorders"). Highly preferred indications include
		T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
			antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
			the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
			transcription factors and modulate	suppressing a T cell-mediated immune response.
			expression of genes involved in	Additional highly preferred indications include
			immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
			assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
			response element that may be used or	disease as described below under "Infectious Disease").
			routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,

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				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
				ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the JURKAT cell line, which is a	
				suspension culture of leukemia cells that	
				produce IL-2 when stimulated.	
185	HGBER72	669	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
			transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
			NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
			element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
			cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
				antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
				the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
				transcription factors and modulate	described below), and immunodeficiencies (e.g., as
				expression of immunomodulatory genes.	described below). An additional highly preferred
-				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
				the NFKB response element that may be	disease as described below under "Infectious Disease").
				used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"). Highly

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				agonists or antagonists of the invention)	preferred indications include neoplasms and cancers, such
				include assays disclosed in Berger et al.,	as, for example, melanoma, renal cell carcinoma,
				Gene 66:1-10 (1998); Cullen and Malm,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Methods in Enzymol 216:362-368 (1992);	pancreatic, esophageal, stomach, brain, liver and urinary
				Henthorn et al., Proc Natl Acad Sci USA	cancer. Other preferred indications include benign
				85:6342-6346 (1988); Black et al., Virus	dysproliferative disorders and pre-neoplastic conditions,
				Gnes 15(2):105-117 (1997); and Fraser et	such as, for example, hyperplasia, metaplasia, and/or
				al., 29(3):838-844 (1999), the contents of	dysplasia. Preferred indications also include anemia,
				each of which are herein incorporated by	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				reference in its entirety. Exemplary human	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				T cells, such as the MOLT4, that may be	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
•				used according to these assays are publicly	granulomatous disease, inflammatory bowel disease,
				available (e.g., through the ATCC).	sepsis, neutropenia, neutrophilia, psoriasis, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, suppression of immune
					reactions to transplanted organs, asthma and allergy.
186	HGBEY14	700	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly

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				polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
187	HGBGN34	701	Production of IL-5	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell Ig production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate B cell Ig production, modulate immune cell	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-5 production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-5 production. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) immunoglobulin production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) immunoglobulin production. A highly preferred indication includes allergy. A highly preferred indication includes asthma. A highly preferred indication includes rhinitis. An additional highly preferred indication is infection (e.g., an infectious

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				polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
				cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
				assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
				proteins evaluate the production of	described below under "Immune Activity", "Blood-
				cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
				stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
				cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
				be used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
				the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
	•			in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
				Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
				al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
				Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
				Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
				Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
				Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
				Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
				contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
				Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				to these assays may be isolated using	immune reactions to transplanted organs and tissues,
		_		techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
				known in the art. Human T cells are	endocarditis, meningitis, and Lyme Disease.
				primary human lymphocytes that mature in	
				the thymus and express a T cell receptor	
				and CD3, CD4, or CD8. These cells	
-				mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
		,		immunomodulatory factors.	
188	HGBHP91	702	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
			DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,

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diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious Diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications associated with insulin resistance.		
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-	21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety.	Adipocytes and pre-adipocytes that may be used according to these assays are publicly
element in adipocytes and pre-adipocytes		

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				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include the mouse 3T3-L1 cell line	
				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
				developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
				like conversion under appropriate	
				differentiation culture conditions.	
189	HGCAC19	703	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
			transcription through	through the CD28 response element are	includes a method for stimulating T cell proliferation. An
			CD28 response element	well-known in the art and may be used or	alternative highly preferred embodiment of the invention
			in immune cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation.
			as T-cells).	polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
				the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
				in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
				transcription through the CD28 response	A highly preferred embodiment of the invention includes a
				element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
				modified to test CD28-response element	An alternative highly preferred embodiment of the
				activity of polypeptides of the invention	invention includes a method for inhibiting (e.g., reducing)
				(including antibodies and agonists or	IL-2 production. Additional highly preferred
				antagonists of the invention) include	indications include inflammation and inflammatory
				assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
				66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
				Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
				85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
				Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. An
				(1997); Parra et al., J Immunol	additional highly preferred indication includes infection
				166(4):2437-2443 (2001); and Butscher et	(e.g., AIDS, and/or as described below under "Infectious
				al., J Biol Chem 3(1):552-560 (1998), the	Disease"). Highly preferred indications include
				contents of each of which are herein	neoplastic diseases (e.g., melanoma, renal cell carcinoma,
				incorporated by reference in its entirety. T	leukemia, lymphoma, and/or as described below under
				cells that may be used according to these	"Hyperproliferative Disorders"). Highly preferred

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indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, pancytopenia, leukopenia, mellide anemia, pancytopenia, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allerey.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a
und cancers, such as, fastatic melanoma), rens al cell carcinoma), all lymphoma), and noreatic, esophageal, ry cancer. Other preferroliferative disorders as, for example, dysplasia. A highly (e.g., tuberculosis, allomatous disease, and us disease as describe e"). A highly preferred of immune reactions is, weitis, psoriasis, ges, uveitis, psoriasis, ges, uveitis, psoriasis, and/lated Disorders", and/lated Disorders", and/lated Disorders", and/lated Disorders, and/lated Disorders, acute lymphoc multiple myeloma, granulomatous disease psis, neutropenia, coagulation, diabetes is, Lyme Disease, asth	of the in cell prolification of the in ment of the ell prolification invention ternative ion includor inactive he invent
indications include neoplasms and cancers, such as, texample, melanoma (e.g., metastatic melanoma), rencarcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other prefeindications include benign dysproliferative disorders pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, an osteoporosis, and/or an infectious disease as describe below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions transplanted organs and/or tissues, uveitis, psoriasis, tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below und "Immune Activity", "Blood-Related Disorders", and/"Cardiovascular Disorders (e.g., as described below und "Immune Activity", and such pancytopenia, leukopenia, humbhoma, arthritis, granulomatous diseass; inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes and allergy.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a
indications include neoplasm example, melanoma (e.g., m carcinoma (e.g., metastatic r leukemia, lymphoma (e.g., T prostate, breast, lung, colon, stomach, brain, liver and uri indications include benign d pre-neoplastic conditions, su hyperplasia, metaplasia, and preferred indication is infect infections associated with gr osteoporosis, and/or an infect below under "Infectious Disc indication is AIDS. Additionation is AIDS. Additionationation is and or titropical spastic paraparesis." "Immune Activity", "Blood" "Cardiovascular Disorders (e.g. "Immune Activity", "Blood" "Cardiovascular Disorders") include anemia, pancytopeni ithrombocytopenia, Hodgkin anemia (ALL), plasmacytom anemia (AL	ferred em d for stim r preferred for inhil embodim ting T ce ment of t activation d embodi
ons incluc a, melano a, lympho b, breast, l b, brain, l ons incluc plastic co asia, meta d indicati ns associa ns associa no is AID on is AID on is AID on is AID on servite plood dis spastic p blood dis anemia, p anemia, p anemia, p s Iympho attory bov itilia, herr i, endocar	ighly pre- ighly pre- ve highly a metho- referred of for activa d embodi
indications example, m carcinoma (leukemia, ly prostate, brs stomach, by indications pre-neoplas hyperplasia preferred in infections a osteoporosis below under indication it indication is indications it ransplanted tropical spaninclude bloc "Immune A "Cardiovass include anentia (AL Burkitt's ly inflammator neutrophilia mellitus, end and allerey.	A h includes alternati includes highly p method preferre for inhil
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cly availa emplary b cording to cording to life of leul hen stimu	ctivation 28 respon 28 respon 29 art and 29 ed to asse 30 the inven 30 stimulate 30 ough the
assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response
assays the AT may be includ suspen produc	Assays throug well-kr routine polype antiboo the inv in T ce transcr
	rough s element s (such
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
	Activation transcripti CD28 resp in immune as T-cells)
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method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. An additional highly preferred indication includes infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia. lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infectiou (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety.	cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.

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				include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allerey.
191 HGCAC19	705	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 160(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include autoinmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. An additional highly preferred indication includes infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under
			cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma),

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			include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and
				pre-neoplastic conditions, such as, for example, hyperplastia, metaplasta, and/or dysplasta. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and
				osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred
				indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and
				સું છ
				"Cardiovascular Disorders"). Preferred indications also include anemia pancytonenia lenkomenia
				thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease.
				inflammatory bowel disease, sepsis, neutropenia,
				neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma
+	100			and allergy.
192 HHEAK45	90/	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			or routinely modified to assess the ability	An additional ingliny prefered indication is a compilication associated with diabetes (e.g., diabetic retinopathy,
			of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
			antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease.
			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
			pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
			glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
			proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., neart disease,

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				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension.
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
				Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
				of each of which is herein incorporated by	with insulin resistance.
				reference in its entirety. Pancreatic cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC) and/or may be routinely generated.	
				Exemplary pancreatic cells that may be	
				used according to these assays include	
				HITT15 Cells. HITT15 are an adherent	
				epithelial cell line established from Syrian	
				hamster islet cells transformed with SV40.	
				These cells express glucagon,	
				somatostatin, and glucocorticoid receptors.	
				The cells secrete insulin, which is	
				stimulated by glucose and glucagon and	
				suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
193	HHEGS55	707	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the

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	ability of nolymentides of the invention	invention metaces a method for summating (e.g., increasing) TME alaba and distinction.
 do 1 - Cello).	(including antibodies and agonists or	include blood disorders (e.g., as described below under
	antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
	the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
	the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
	growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
	transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
	used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
	activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
	invention (including antibodies and	immune response. Additional highly preferred indications
 -	agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
	include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
	Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
	Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
	Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
	85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
	Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
	content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
	incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
	cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
	assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
	the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
	may be used according to these assays	pre-neoplastic conditions, such as, for example,
	include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
	2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
	with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
		anemia (ALL), plasmacytomas, multiple myeloma,
		Burkitt's lymphoma, arthritis, AIDS, granulomatous
		disease, inflammatory bowel disease, neutropenia,
		neutrophilia, psoriasis, suppression of immune reactions to
		transplanted organs and tissues, hemophilia,
		hypercoagulation, diabetes mellitus, endocarditis,
		<i>(</i>
		asthma and allergy. An additional preferred indication
		is infection (e.g., an infectious disease as described below
		under "Infectious Disease").

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194 HHEOW19	708	Production of	MIP-Talpha FMAT. Assays for	A highly preferred embodiment of the invention
		mart raibita	activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
			monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
			chemotaxis are well known in the art and	production. A highly preferred indication is infection
			may be used or routinely modified to	(e.g., an infectious disease as described below under
			assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
			invention (including antibodies and	blood disorders (e.g., as described below under "Immune
			agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
			mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
			chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
			differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
			for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
-			the production of chemokines, such as	described below). Additional highly preferred indications
			macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				Preferred indications also include anemia, pancytopenia,
			monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
			modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
			invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
			include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
			J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
			204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
			a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
			(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
			Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
			al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
			Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
			2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
			Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
			each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
			reference in its entirety. Human dendritic	dysplasia.
			cells that may be used according to these	
			assays may be isolated using techniques	
			disclosed herein or otherwise known in the	

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				art Human dendritic cells are antioen	
				presenting cells in suspension culture	
				which when optimized by entiron and/or	
				which, when acuvated by antigen and/or cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
194	HHEOW19	708	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
		·		response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
		•••		Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
				(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,

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				Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are	granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its entirety. Human dendritic cells that may	immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				definition cells are affiliagen presenting cells	infectious disease as described below under infectious
				activated by antigen and/or cytokines,	Disease).
				initiate and upregulate T cell proliferation and functional activities.	
194	HHEOW19	708	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
	_			of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
	***			modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include

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weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional
Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for
	Upregulation of T cells and activation of T cells
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				immunomodulatory proteins evaluate the	highly preferred indications include infection. Preferred
				as CD71, and the activation of T cells.	Indications include helphastic diseases (e.g., feukeima, lymphoma, and/or as described below under
				Such assays that may be used or routinely	"Hyperproliferative Disorders"). Preferred indications
				modified to test immunomodulatory	include neoplasms and cancers, such as, for example,
		•		activity of polypeptides of the invention	leukemia, lymphoma, melanoma, and prostate, breast,
				(including antibodies and agonists or	lung, colon, pancreatic, esophageal, stomach, brain, liver
				antagonists of the invention) include, for	and urinary cancer. Other preferred indications include
				example, the assays disclosed in Miraglia	benign dysproliferative disorders and pre-neoplastic
				et al., J Biomolecular Screening 4:193-204	conditions, such as, for example, hyperplasia, metaplasia,
				(1999); Rowland et al., "Lymphocytes: a	and/or dysplasia. Preferred indications include anemia,
				practical approach" Chapter 6:138-160	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				(2000); and Afetra et al., Ann Rheum Dis	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				52(6):457-460 (1993), the contents of each	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
				reference in its entirety. Human T cells	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				that may be used according to these assays	immune reactions to transplanted organs and tissues,
				may be isolated using techniques disclosed	hemophilia, hypercoagulation, diabetes mellitus,
				herein or otherwise known in the art.	endocarditis, meningitis, Lyme Disease, and asthma and
				Human T cells are primary human	allergy.
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
961	HHFFL34	710	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies

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			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
			invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
			the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
			may be used according to these assays	pre-neoplastic conditions, such as, for example,
			include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
			2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
		-	with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma,
				Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, neutropenia,
				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
+	1	- - - - -		under Infectious Disease").
19/ HHFFS40	11/	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention
		Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
•			may be used or routinely modified to	An alternative highly preferred embodiment of the
			assess the ability of polypeptides of the	invention includes a method for inhibiting endothelial cell
			invention (including antibodies and	growth. A highly preferred embodiment of the
			agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
			promote caspase protease-mediated	cell proliferation. An alternative highly preferred
			apoptosis. Induction of apoptosis in	embodiment of the invention includes a method for

 endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly
 regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
apoptosis that may be used or routinely	includes a method for inhibiting (e.g., decreasing)
modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
of polypeptides of the invention (including	embodiment of the invention includes a method for
 antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
the invention) include the assays disclosed	embodiment of the invention includes a method for
in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
 Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
 the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
endothelial cells which line blood vessels	overload, and/or as described below under
and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,

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					5		ځ.							na;		9	يو	on		pic		Additional highly		ive		ent		s,		p			"Cardiovascular Disorders"). Preferred indications include	.ల	ğ	£ €
		na,	20	<u>.</u>	pancreatic, esophageal, stomach, brain, liver, and urinary		dysproliferative disorders and pre-neoplastic conditions,	L	dysplasia. Highly preferred indications also include	Ä,			ers	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon		fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	hig		diabetic or other retinopathies, thrombotic and coagulative		disorders, age-related macular degeneration, and treatment		Additional highly preferred indications include fibromas,	_	Preferred indications include blood			incl	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described	below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and
		angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	5 5		diti	such as, for example, hyperplasia, metaplasia, and/or	ոշր	arterial disease, such as, atherosclerosis, hypertension,	Š,		aneurysms, restenosis; venous and lymphatic disorders	she	ascı	ons	ă	m b	Ħ	enu	inc	nal	'n,	agi	Ę	tre	ns.	pro	heart disease, cardiac arrest, heart valve disease, and	de 1	ဥ		ns	syst	des	d b
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	bacillary angiomatosis, hemangioendothelioma,	arc	ang	ပ္သံ : မ	äti	cancer. Preferred indications include benign	olife.	s, f	sia.	l di	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	/sm	s th	þer	e,	e tr	/asc	angioplasty, and atheroschlerotic lesions), implant	n, s	is, c	acute renal failure, and osteoporosis.	preferred indications include stroke, graft rejection,	္ပ	disorders, vascularitis, lymph angiogenesis, sexual	ers,	/prevention of endometriosis and related conditions.	ona	lise	vascular disease.	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	0.02	Ē	ž,	an (
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					inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
197	HHFFS40	711	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts,	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred
				smooth muscle, and other cell types that exert a wide variety of inflammatory and	embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are well known in the art and may be used or	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of polypeptides of the invention (including	Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of the invention) to mediate	(e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				assays that test for immunomodulatory	suppressing a T cell-mediated infillure response, and suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor alpha (TNFa), and the induction or	inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
		-		response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				rounnely modulaed to test immunomodulatory activity of	leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				Miraglia et al., J Biomolecular Screening	mangnant gnoma, solid tumors, and prostate, oreast, lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				(1198); Dahlen et al., J Immunol	pancytopenia. I referred more aneima, pancytopenia. Hodokin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
				(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of

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				herein incorporated by reference in its	immune reactions to transplanted organs and tissues.
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation and functional activities.	
197	HHFFS40	711	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
,				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated

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			entirety. Pancreatic cells that may be used	with insulin resistance
-			according to these assays are publicly	
			available (e.g., through the ATCC) and/or	
			may be routinely generated. Exemplary	
			pancreatic cells that may be used	
			according to these assays include HITT15	
			Cells. HITT15 are an adherent epithelial	
			cell line established from Syrian hamster	
			islet cells transformed with SV40. These	
			cells express glucagon, somatostatin, and	
			glucocorticoid receptors. The cells secrete	
••••			insulin, which is stimulated by glucose and	
			glucagon and suppressed by somatostatin	
			or glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
			Sci. USA 78: 4339-4343, 1981.	
198 HHGCS78	712	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
		transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
		DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
		element in adipocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
		and pre-adipocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
			antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
			the invention) to activate the DMEF1	neuropathy, nerve disease and nerve damage (e.g., due to
_			response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
			(such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
			promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
			production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
			element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
			and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
			another transcription factor that is required	stroke, and other diseases and disorders as described in the
			for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
			in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
			insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
			fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
			that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
			test for DMEF1 response element activity	diseases and disorders as described in the "Infectious

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			(in adipocytes and pre-adipocytes) by polypeptides of the invention (including	tion t
			antibodies and agonists or antagonists of the invention) include assays disclosed	contracture). An additional highly preferred indication is obesity and/or complications associated with
			inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
			273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
-		-1-	J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
	-		M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
			21 (1994); "Identification of a 30-base pair	
			regulatory element and novel DNA	
			binding protein that regulates the human	
			GLUT4 promoter in transgenic mice", J	
			Biol Chem. 2000 Aug 4;275(31):23666-	
	*		73; Berger, et al., Gene 66:1-10 (1988);	
			and, Cullen, B., et al., Methods in	
			Enzymol. 216:362–368 (1992), the	
			contents of each of which is herein	
			incorporated by reference in its entirety.	
			Adipocytes and pre-adipocytes that may be	
			used according to these assays are publicly	
			available (e.g., through the ATCC) and/or	
			may be routinely generated. Exemplary	
			cells that may be used according to these	
			assays include the mouse 3T3-L1 cell line	
			which is an adherent mouse preadipocyte	
			cell line. Mouse 3T3-L1 cells are a	
			continuous substrain of 3T3 fibroblasts	
			developed through clonal isolation. These	
			cells undergo a pre-adipocyte to adipose-	
			like conversion under appropriate	
\dashv			differentiation culture conditions.	
198 HHGCS78	8 712	Production of ICAM-1	Assays for measuring expression of	Preferred embodiments of the invention include using
			ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
		-	may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
			assess the ability of polypeptides of the	and/or treatment of Inflammation, Vascular Disease,
			invention (including antibodies and	Athereosclerosis, Restenosis, and Stroke
			agonists or antagonists of the invention) to	

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199 HHGDT26	713	Activation of transcription through API response element in immune cells (such as T-cells).	regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC). Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element activity of polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications shown and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign
			Biol Chem 2/2(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986- 4993 (1998); and Fraser et al., Eur J	dysproliterative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis.

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				[mmiino] 20/3):838-844 (1999) the	sethma AIDS allermy anemia nanoutonenia leukonenia
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
100	UUCNTOK	713	Activition	with cytotoxic acutylity.	A
661	07 I QDUU	/13	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Kesponse Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,

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				publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease")
500	HHPFU28	714	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. The alls that may be used.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and accepts the propertical indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors,

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		assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
	Endothelial Cell ERK Signaling Pathway.	an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang	A figury preterred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a
		and Karin, Nature 410(6824):37-40	method for stimulating endothelial cell differentiation. An

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by reterence in its entirety. Endothelia cells that may be used according to the assays are publicly available (e.g., into the ATCC). Exemplary endothelial cells that may be used according to these as include human umbilical vein endothelial cells which line venous blood vessels, are involved in functions that include, are not limited to, angiogenesis, vascul permeability, vascular tone, and immuncell extravasation.	ed ents with the says says and put we had and says says and says says says says says says says say	differentiation. A highly preferred embodiment of the invention includes a method for stimulating angiogensis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular pisorders"). Highly preferred indications that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma.	T 0 0
	ang	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	

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ung, colon, ver, and urinary	tic conditions,	sia, and/or	s also include	ypertension,	pulitides,	enom,	tic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	heral vascular	ndications also	l injured tissue	(e.g., vascular injury such as, injury resulting from balloon	implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	eases such as	Additional highly	rejection,	diabetic or other retinopathies, thrombotic and coagulative	s, sexual	disorders, age-related macular degeneration, and treatment	onditions.	lude fibromas,	sease, and	s include blood	'Immune	/or	"Cardiovascular Disorders"). Preferred indications include	hritis, systemic	lupus erythematosis, multiple sclerosis and/or as described	below) and immunodeficiencies (e.g., as described below).	Additional preferred indications include inflammation and	chronic	bowel disease	J.
include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benion	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	lymphangitis, an	and other vascular disorders such as peripheral vascular	Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	as, injury resulti	angioplasty, and atheroschlerotic lesions), implant	1 reperfusion inj	arthritis, cerebrovascular disease, renal diseases such as	eoporosis. A	preferred indications include stroke, graft rejection,	iies, thrombotic	disorders, vascularitis, lymph angiogenesis, sexual	ular degeneratio	/prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,	heart disease, cardiac arrest, heart valve disease, and	Preferred indications include blood	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	"). Preferred in	autoimmune diseases (e.g., rheumatoid arthritis, systemic	ole sclerosis and	ncies (e.g., as de	tions include in	inflammatory disorders (such as acute and chronic	inflammatory diseases, e.g., inflammatory bowel disease	and Crohn's disease), and pain management
icers such as, presophageal, sto	ative disorders	r example, hype	Highly prefe	ease, such as, at	rtery disease, inf	disease and Rey	restenosis; ven	ombophlebitis, 1	ascular disorder		ıma such as wou	ılar injury such a	', and atheroschl	arring, ischemia	rebrovascular d	acute renal failure, and osteoporosis.	rdications includ	other retinopath	ascularitis, lym	ige-related macı	of endometrios	highly preferred	diac		e.g., as describe	'Blood-Related	cular Disorders'	e diseases (e.g.,	ematosis, multip	immunodeficie	preferred indica	ry disorders (su	ry diseases, e.g.	c disease) and r
include can pancreatic,	dysprolifer	such as, for	dysplasia.	arterial dise	coronary ar	Reynaud's o	aneurysms,	such as thro	and other v	disease, and cancer.	include trau	(e.g., vascu	angioplasty	fixation, sc	arthritis, ce	acute renal	preferred in	diabetic or	disorders, v	disorders, a	/prevention	Additional	heart diseas	vascular disease.	disorders (e	Activity", "	"Cardiovas	autoimmun	lupus erythe	below) and	Additional	inflammato	inflammator	and Crohn'
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201	HHPSA85	715	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention	\Box
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.	
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the	
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte	
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the	
	-			assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte	
				invention (including antibodies and	differentiation. An alternative highly preferred	
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for	
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly	
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method	
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An	
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention	
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,	
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly	
				agonists or antagonists of the invention)	=	
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").	_
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic	
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described	
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred	
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,	
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart	
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below	
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",	
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders	
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural	
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity	
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as	
				publicly available (e.g., through the	described below under "Infectious Disease").	
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An	
				that may be used according to these assays	additional highly preferred indication is a complication	
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,	
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,	
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as	
				cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic	
				and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to	
				like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,	-
				differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or	

					blood vessel blockage), seizures, mental confusion.
				-	drowsiness, nonketotic hyperglycemic-hyperosmolar
					coma, cardiovascular disease (e.g., heart disease,
-					atherosclerosis, microvascular disease, hypertension,
					stroke, and other diseases and disorders as described in the
					"Cardiovascular Disorders" section below), dyslipidemia,
					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infection (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below (particularly of the urinary tract
					and skin). An additional highly preferred indication is
					obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					plicat
					insulin resistance. Additional highly preferred
-					orders
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include, hypertension, coronary artery disease,
					dyslipidemia, gallstones, osteoarthritis, degenerative
					arthritis, eating disorders, fibrosis, cachexia, and kidney
					diseases or disorders. Preferred indications include
					neoplasms and cancer, such as, lymphoma, leukemia and
					breast, colon, and kidney cancer. Additional preferred
					indications include melanoma, prostate, lung, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer.
					Highly preferred indications include lipomas and
					liposarcomas. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
		······································			such as, for example, hyperplasia, metaplasia, and/or
					dysplasia.
202	HHSBI06	716		Caspase Apoptosis. Assays for caspase	A highly preferred indication is diabetes mellitus.
			in pancreatic beta cells.	apoptosis are well known in the art and	An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,

described in the "Renal Disorders" section below), diabetic stroke, and other diseases and disorders as described in the Diseases" section below, especially of the urinary tract and diabetic neuropathy), blood vessel blockage, heart disease, Disorders" section below), neuropathy, vision impairment neuropathy, nerve disease and nerve damage (e.g., due to indication is obesity and/or complications associated with "Cardiovascular Disorders" section below), dyslipidemia, highly preferred indications are complications associated obesity. Additional highly preferred indications include diabetic nephropathy, kidney disease (e.g., renal failure, impaired wound healing, and infection (e.g., infectious stroke, impotence (e.g., due to diabetic neuropathy or diseases and disorders as described in the "Infectious atherosclerosis, microvascular disease, hypertension, drowsiness, nonketotic hyperglycemic-hyperosmolar (e.g., diabetic retinopathy and blindness), ulcers and endocrine disorders (as described in the "Endocrine nephropathy and/or other diseases and disorders as blood vessel blockage), seizures, mental confusion, An additional highly preferred coma, cardiovascular disease (e.g., heart disease, skin), carpal tunnel syndrome and Dupuytren's weight loss or alternatively, weight gain. with insulin resistance. contracture). agonists or antagonists of the invention) to routinely modified to test capase apoptosis al., Br J Pharmacol, 129(4):687-94 (2000); apoptosis. Apoptosis in pancreatic beta is entirety. Pancreatic cells that may be used associated with induction and progression FEBS Lett, 459(2):238-43 (1999); Zhang, Harlan, J Atheroscler Thromb 3(2): 75-80 available (e.g., through the ATCC) and/or 39(6):1229-36 (1996); Krautheim, A., et ::S44-7 (2001); Suk K, et al., J Immunol, (1996); the contents of each of which are according to these assays include RIN-m. activity of polypeptides of the invention antagonists of the invention) include the may be routinely generated. Exemplary radiation induced transplantable rat islet FEBS Lett, 400(3):285-8 (1997); Saini, RIN-m is a rat adherent pancreatic beta assess the ability of polypeptides of the 37(3): 209-218 (2000); and Karsan and cell insulinoma cell line derived from a assays disclosed in: Loweth, AC, et al., 166(7):4481-9 (2001); Tejedo J, et al., (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res herein incorporated by reference in its caspase apoptosis that may be used or according to these assays are publicly including antibodies and agonists or Chandra J, et al., Diabetes, 50 Suppl promote caspase protease-mediated of diabetes. Exemplary assays for S., et al., FEBS Lett, 455(3):315-20 invention (including antibodies and KS, et al., Biochem Mol Biol Int, pancreatic cells that may be used

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203	HHSB165	717	Production of ICAM-1	cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1980 77:3519. Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely senerated. Exemplary cells that	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
				used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	
503	HHSB165	717	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic

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	promote caspase protease-mediated	neuropathy, nerve disease and nerve damage (e.g., due to
	apoptosis. Apoptosis in pancreatic beta is	diabetic neuropathy), blood vessel blockage, heart disease,
	associated with induction and progression	stroke, impotence (e.g., due to diabetic neuropathy or
	of diabetes. Exemplary assays for	blood vessel blockage), seizures, mental confusion,
	caspase apoptosis that may be used or	drowsiness, nonketotic hyperglycemic-hyperosmolar
	routinely modified to test capase apoptosis	coma, cardiovascular disease (e.g., heart disease,
	activity of polypeptides of the invention	atherosclerosis, microvascular disease, hypertension,
-	(including antibodies and agonists or	stroke, and other diseases and disorders as described in the
	antagonists of the invention) include the	"Cardiovascular Disorders" section below), dyslipidemia,
	assays disclosed in: Loweth, AC, et al.,	endocrine disorders (as described in the "Endocrine
	FEBS Lett, 400(3):285-8 (1997); Saini,	Disorders" section below), neuropathy, vision impairment
	KS, et al., Biochem Mol Biol Int,	(e.g., diabetic retinopathy and blindness), ulcers and
	39(6):1229-36 (1996); Krautheim, A., et	impaired wound healing, and infection (e.g., infectious
	al., Br J Pharmacol, 129(4):687-94 (2000);	diseases and disorders as described in the "Infectious
	Chandra J, et al., Diabetes, 50 Suppl	Diseases" section below, especially of the urinary tract and
	1:S44-7 (2001); Suk K, et al., J Immunol,	skin), carpal tunnel syndrome and Dupuytren's
	166(7):4481-9 (2001); Tejedo J, et al.,	contracture). An additional highly preferred
	FEBS Lett, 459(2):238-43 (1999); Zhang,	besit
	S., et al., FEBS Lett, 455(3):315-20	obesity. Additional highly preferred indications include
	(1999); Lee et al., FEBS Lett 485(2-3):	weight loss or alternatively, weight gain. Aditional
	122-126 (2000); Nor et al., J Vasc Res	highly preferred indications are complications associated
	37(3): 209-218 (2000); and Karsan and	with insulin resistance.
	Harlan, J Atheroscler Thromb 3(2): 75-80	
	(1996); the contents of each of which are	
	herein incorporated by reference in its	
	entirety. Pancreatic cells that may be used	
	according to these assays are publicly	
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	pancreatic cells that may be used	
	according to these assays include RIN-m.	
	RIN-m is a rat adherent pancreatic beta	
	cell insulinoma cell line derived from a	
	radiation induced transplantable rat islet	
	cell tumor. The cells produce and secrete	
	islet polypeptide hormones, and produce	
	insulin, somatostatin, and possibly	

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				glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
204	HHSDI53	718	Activation of transcription through serum response element in immune cells (such	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routingly modified to assess the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes mathod for attending (e.g., reducing for the production).
			as T-cells).	ability of polypeptides of the invention (including antibodies and agonists or	increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under
		·		anagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis.
				growth. Exemplary assays for transcription through the SRE that may be	systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below) imminodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the invention (including antibodies and	immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				cells that may be used according to these	incianonia, gnoria (e.g., mangnam gnoma), sono tumors, and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				may be used according to these assays	mucations include beingn dyspromerative disorders and pre-neoplastic conditions, such as, for example
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
		,		2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), piasmacytomas, mutupie myetoma, Burkitt's lymphoma, arthritis, ATDS, grannlomatons
					disease, inflammatory bowel disease, neutropenia,

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					neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infections disease as described below
					under "Infectious Disease").
204	HHSDI53	718	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins secreted by	includes a method for inhibiting (e.g., reducing) IL-5
				TH2 cells, mast cells, basophils, and	production. An alternative highly preferred embodiment of
				eosinophils that stimulate eosinophil	the invention includes a method for stimulating (e.g.,
				function and B cell Ig production and	increasing) IL-5 production. A highly preferred
				promote polarization of CD4+ cells into	embodiment of the invention includes a method for
				TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
				may be used or routinely modified to	An alternative highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for inhibiting (e.g.,
				invention (including antibodies and	decreasing) immunoglobulin production. A highly
				agonists or antagonists of the invention) to	preferred indication includes allergy. A highly
				mediate immunomodulation, stimulate	preferred indication includes asthma. A highly
				immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
				production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
				polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
				cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
		· · · · · ·		assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
				proteins evaluate the production of	described below under "Immune Activity", "Blood-
				cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
				stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
				cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
				be used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
				the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
				in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
				Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
				al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include

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-				Blood 92(9):3338-3345 (1998); Jung et al., Eur J Immunol 25(8):2413-2416 (1995); Mori et al., J Allergy Clin Immunol 106(1 Pt 2):558-564 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
502	HHSFC09	719	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include

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systemic lupus erythematosis, and multiple	lupus erythematosis, multiple sclerosis and/or as described
sclerosis). Assays for immunomodulatory	below) and immunodeficiencies (e.g., as described below),
proteins expressed on MHC class II	boosting a T cell-mediated immune response, and
expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
cells are well known in the art and may be	response. A highly preferred indication is diabetes
used or routinely modified to assess the	mellitus. An additional highly preferred indication
ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
 assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
 approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
the contents of each of which are herein	are complications associated with insulin resistance.
incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
to these assays may be isolated using	dystrophy, and/or as described herein.
techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,
known in the art. Human T cells are	and/or as described below under "Infectious Disease").

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Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment
primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of the
	Regulation of viability and proliferation of pancreatic beta cells.
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	HILCA24
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				invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
207	HILCA24	721	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element that may be	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred

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				polypeptides of the invention (including antibodies and agonists or antagonists of	indications include neoplasms and cancers, such as, leukemia. Ivmphoma. melanoma. and prostate. breast.
				the invention) include assays disclosed in	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	as, for exam
				George et al. 1004 03:0342-0340 (1900);	and/or dysplasia. Preferred indications include
				(1009): Moffett of all Transplatetion	ancinia, pancytopenia, reukopenia, untombocytopenia,
				(1996); Moltaut et al., Transplantauon (607):1501-1503 (2000): Curiel et al. Eur	riodgkin s disease, acute lymphocytic anemia (ALL),
				J Immunol 27(8):1982-1987 (1997): and	prasmacytomas, munipic mycioma, burkitt s rympnoma, arthritis AIDS orannlomatons disease inflammatory
				Masuda et al., J Biol Chem	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				275(38):29331-29337 (2000), the contents	suppression of immune reactions to transplanted organs
				of each of which are herein incorporated	and tissues, hemophilia, hypercoagulation, diabetes
				by reference in its entirety. T cells that	mellitus, endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays are	An additional preferred indication is infection (e.g., an
				publicly available (e.g., through the	infectious disease as described below under "Infectious
				ATCC). Exemplary T cells that may be	Disease").
				used according to these assays include the	
				HT2 cell line, which is an IL-2 dependent	
				suspension culture of T cells that also	
				respond to IL-4.	
207 HIL	HILCA24	721	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
	2 181		transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
	-			assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
		1, ,,,		modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
	-			used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
				response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,

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				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
				the invention) include assays disclosed in Berger et al. Gene 66:1-10 (1998): Cullen	lung, colon, pancreatic, esophageal, stomach, brain, liver
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	conditions, such as, for example, hyperplasia, metaplasia,
				Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications
				Georas et al., Blood 92(12):4529-4538	include anemia, pancytopenia, leukopenia,
				(1998); Moffatt et al., Transplantation	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				69(7):1521-1523 (2000); Curiel et al., Eur	anemia (ALL), plasmacytomas, multiple myeloma,
				J Immunol 27(8):1982-1987 (1997); and	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				Masuda et al., J Biol Chem	disease, inflammatory bowel disease, sepsis, neutropenia,
				275(38):29331-29337 (2000), the contents	neutrophilia, psoriasis, suppression of immune reactions to
				of each of which are herein incorporated	transplanted organs and tissues, hemophilia,
				by reference in its entirety. T cells that	hypercoagulation, diabetes mellitus, endocarditis,
				may be used according to these assays are	meningitis, and Lyme Disease. An additional
				publicly available (e.g., through the	preferred indication is infection (e.g., an infectious disease
				ATCC). Exemplary T cells that may be	as described below under "Infectious Disease").
				used according to these assays include the	
				SUPT cell line, which is a suspension	
				culture of IL-2 and IL-4 responsive T cells.	
708	HILCA24	722	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
			and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
			pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
				routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
				proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
				example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment

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208 HILCA24	722	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167. Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of multiple genes.	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. A highly preferred indication is allergy. A highly preferred indication is allergy. Additional highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and multiple sclerosis and/or as described below) and
			the STAT6 response element that may be used or routinely modified to test STAT6	Preferred indications (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described
			response element activity of the	below under "Hyperproliferative Disorders") Preferred

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				polypeptides of the invention (including	indications include neoplasms and cancers, such as,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
				the invention) include assays disclosed in	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	as, for exam
		•		Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications include
				Georas et al., Blood 92(12):4529-4538	anemia, pancytopenia, leukopenia, thrombocytopenia,
				(1998); Moffatt et al., Transplantation	Hodgkin's disease, acute lymphocytic anemia (ALL),
				69(7):1521-1523 (2000); Curiel et al., Eur	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
			·	J Immunol 27(8):1982-1987 (1997); and	arthritis, AIDS, granulomatous disease, inflammatory
			•	Masuda et al., J Biol Chem	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				275(38):29331-29337 (2000), the contents	suppression of immune reactions to transplanted organs
				of each of which are herein incorporated	and tissues, hemophilia, hypercoagulation, diabetes
				by reference in its entirety. T cells that	mellitus, endocarditis, meningitis, and Lyme Disease.
				may be used according to these assays are	An additional preferred indication is infection (e.g., an
				publicly available (e.g., through the	infectious disease as described below under "Infectious
				ATCC). Exemplary T cells that may be	Disease").
				used according to these assays include the	
				HT2 cell line, which is an IL-2 dependent	
×				suspension culture of T cells that also	
				respond to IL-4.	
208 HILO	HILCA24	722	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
			transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
-				assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
•				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
				modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
				used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
				response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,

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				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	conditions, such as, for example, hyperplasia, metaplasia,
				Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications
				Georas et al., Blood 92(12):4529-4538	include anemia, pancytopenia, leukopenia,
				(1998); Moffatt et al., Transplantation	thrombocytopenia, Hodgkin's disease, acute lymphocytic
·				69(7):1521-1523 (2000); Curiel et al., Eur	anemia (ALL), plasmacytomas, multiple myeloma,
				J Immunol 27(8):1982-1987 (1997); and	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				Masuda et al., J Biol Chem	disease, inflammatory bowel disease, sepsis, neutropenia,
				275(38):29331-29337 (2000), the contents	neutrophilia, psoriasis, suppression of immune reactions to
				of each of which are herein incorporated	transplanted organs and tissues, hemophilia,
				by reference in its entirety. T cells that	hypercoagulation, diabetes mellitus, endocarditis,
				may be used according to these assays are	meningitis, and Lyme Disease. An additional
				publicly available (e.g., through the	preferred indication is infection (e.g., an infectious disease
				ATCC). Exemplary T cells that may be	as described below under "Infectious Disease").
				used according to these assays include the	
				SUPT cell line, which is a suspension	
				culture of IL-2 and IL-4 responsive T cells.	
508	HISAT67	723	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
-				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment

			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
			Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
			(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
			Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
			Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
			865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
			Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
			Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
			Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
			of each of which is herein incorporated by	with insulin resistance.
	-		reference in its entirety. Pancreatic cells	
			that may be used according to these assays	
			are publicly available (e.g., through the	
			ATCC) and/or may be routinely generated.	
		-	Exemplary pancreatic cells that may be	
			used according to these assays include	
			HITT15 Cells. HITT15 are an adherent	
			epithelial cell line established from Syrian	
			hamster islet cells transformed with SV40.	
			These cells express glucagon,	
			somatostatin, and glucocorticoid receptors.	
			The cells secrete insulin, which is	
			stimulated by glucose and glucagon and	
			suppressed by somatostatin or	
			glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
210 HJBCU75	724	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
		and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
		pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
			antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
			the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
			proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,

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				example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
	-			viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
				(1998), the contents of each of which is	obesity. Additional highly preferred indications include
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	tions ass
	-			according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
		·		characteristics typical of native pancreatic	
				beta cells including glucose inducible	
_				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
211	HJMAA03	725	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		•	transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications

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				(including antibodies and agonists or	include blood disorders (e.g. as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
-				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
		-		85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
-				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
211	HJMAA03	725	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication

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	pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
		of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
		antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
		the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
		secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
		is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
		insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
		pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
		glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
		proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
		key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
		assays that may be used or routinely	stroke, and other diseases and disorders as described in the
		modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
		secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
-		polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
		antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
		the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
		Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
		2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
		Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
		Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
		(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
		Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
		(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
		herein incorporated by reference in its	highly preferred indications are complications associated
		entirety. Pancreatic cells that may be used	with insulin resistance.
		according to these assays are publicly	
		available (e.g., through the ATCC) and/or	
	***	may be routinely generated. Exemplary	
		pancreatic cells that may be used	
		according to these assays include rat INS-1	
		cells. INS-1 cells are a semi-adherent cell	
		line established from cells isolated from an	
		X-ray induced rat transplantable	
		insulinoma. These cells retain	
		characteristics typical of native pancreatic	
		beta cells including glucose inducible	

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				insulin secretion. References: Asfari et al. Endocrinology 1992 130:167	
212	HJMAV41	726	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
•				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,

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					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
		-· <u>-</u>			is infection (e.g., an infectious disease as described below under "Infections Disease.")
212	HJMAV41	726	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by T cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., reducing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity, and	boosting a T cell-mediated immune response, and
				mediate humoral and/or cell-mediated	suppressing a T cell-mediated immune response.
				immunity. Exemplary assays that test for	Additional highly preferred indications include
				immunomodulatory proteins evaluate the	inflammation and inflammatory disorders, and treating
				production of cytokines such as tumor	joint damage in patients with rheumatoid arthritis. An
				necrosis factor alpha (TNFa), and the	additional highly preferred indication is sepsis. Highly
				induction or inhibition of an inflammatory	preferred indications include neoplastic diseases (e.g.,
				or cytotoxic response. Such assays that	leukemia, lymphoma, and/or as described below under
				may be used or routinely modified to test	"Hyperproliferative Disorders"). Additionally, highly
				immunomodulatory activity of	preferred indications include neoplasms and cancers, such
				polypeptides of the invention (including	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				antibodies and agonists or antagonists of	malignant glioma), solid tumors, and prostate, breast, lung,
				the invention) include assays disclosed in	colon, pancreatic, esophageal, stomach, brain, liver and
				Miraglia et al., J Biomolecular Screening	urinary cancer. Other preferred indications include benign
				4:193-204 (1999); Rowland et al.,	dysproliferative disorders and pre-neoplastic conditions,
				"Lymphocytes: a practical approach"	such as, for example, hyperplasia, metaplasia, and/or
				Chapter 6:138-160 (2000); Verhasselt et	dysplasia. Preferred indications include anemia,
				al., Eur J Immunol 28(11):3886-3890	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				(1198); Dahlen et al., J Immunol	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				160(7):3585-3593 (1998); Verhasselt et	multiple myeloma, Burkitt's lymphoma, arthritis, asthma,

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				al., J Immunol 136:2919-2923 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to	disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
213	HJMAY90	727	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992), Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al.,	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indication is neclose sec.; leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the content of each of which are herein	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,

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disorders. Additional highly preferred indications include asthma and allergy Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma,	melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic attenta (ALL), multiple myeloma, burkitt s lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred	nfe us	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities.	Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these	assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for the invention through the AP1 assays for
				Activation of transcription through AP1 response element in immune cells (such as T-cells).
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				alement that may be used or routinely	imminotoficiania (a r a described halow) Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
214	HJPBE39	728	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
			transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
			cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
			element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
			cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
				antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
				the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
				regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
				modulate expression of genes involved in a	described below), boosting a T cell-mediated immune
				wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under

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				66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
214	НЈРВЕ39	728	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below

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			85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, moditions to disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
214 HJPBE39	728	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

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215	HJPBK28	729	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"]. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs,
216	Н.РСН08	730	Proliferation, differentiation, and/or cytokine production in immune cells (such as	suspension culture of IL-2 and IL-4 responsive T cells. Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or	asthma and allergy. Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation infection, allered
			T-cells).	routinely modified to assess the ability of	asthma, autoimmunity, and cancer.

polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation, and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakanoto H, et al., J Biol Chem, 275(46):35867-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the mouse CTLL cell line.	
	Activation of Adipocyte ERK Signaling Pathway
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al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1996); Le Marchand-Brustel 1; Exp Clin Endocrinol Diabetes 107(2):126-132	diseases (e.g., iipomas, iiposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	sec
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
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	or alternatively, weight gain. Additional highly

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218 HKACI79	732	Upregulation of CD152 and activation of T cells	expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity," "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,

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				imminomodulatory protains avaluate the	highly professed indications include accompany
		··· ,		minimination of the control of the c	inging preferred indications include incopiasins and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
.,				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
-				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
-				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
		-		Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to imminomodulatory factors	
218 HK	HKACI79	732	Upregulation of HLA-	HLA-DR FMAT. MHC class II is essential	Highly preferred indications include blood disorders
			DR and activation of T	for correct presentation of antigen to CD4+	(e.g., as described below under "Immune Activity",
			cells	T cells. Deregulation of MHC class II has	"Blood-Related Disorders", and/or "Cardiovascular
				been associated with autoimmune diseases	Disorders"). Highly preferred indications include
				(e.g., diabetes, rheumatoid arthritis,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				systemic lupus erythematosis, and multiple	lupus erythematosis, multiple sclerosis and/or as described
				sclerosis). Assays for immunomodulatory	below) and immunodeficiencies (e.g., as described below),
	1,000			proteins expressed on MHC class II	boosting a T cell-mediated immune response, and

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	expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
	cells are well known in the art and may be	response. A highly preferred indication is diabetes
-	used or routinely modified to assess the	
	ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
	(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
	antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
	the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
	humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
	Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
	immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
	upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
	such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
	activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
	be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
	immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
	polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
	antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
	the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
	assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
	Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
	Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
	approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
	Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
	89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
	Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
	Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
	117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
	Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
	the contents of each of which are herein	are complications associated with insulin resistance.
	incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
	Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
	to these assays may be isolated using	dystrophy, and/or as described herein.
	techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,
	known in the art. Human T cells are	and/or as described below under "Infectious Disease").
	primary human lymphocytes that mature in	Preferred indications include endocrine disorders (e.g., as
	the thymus and express a T Cell receptor	described below under "Endocrine Disorders"), and
	and CD3, CD4, or CD8. These cells	neoplastic diseases (e.g., leukemia, lymphoma, and/or as

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			mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and
219 HKAFF50	733	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) LL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) LL-2 production. Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.

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				(1997); Parra et al., J Immunol	additional highly preferred indication includes infection
				al., J Biol Chem 3(1):552-560 (1998), the	Disease"). Highly preferred indications include
				contents of each of which are herein	neoplastic diseases (e.g., melanoma, renal cell carcinoma,
				incorporated by reference in its entirety. T	leukemia, lymphoma, and/or as described below under
		-		cells that may be used according to these	Hyperproliferative Disorders"). Highly preferred
				the ATCC Examples, himon T call that	indications include neoplasms and cancers, such as, for
				may be used according to these assays	carrinoma (e.g., metastatic ranal call concinoma)
· · · ·		·		include the JURKAT cell line, which is a	leukemia, lymphoma (e.g., T cell lymphoma), and
				suspension culture of leukemia cells that	prostate, breast, lung, colon, pancreatic, esophageal,
				produce IL-2 when stimulated.	stomach, brain, liver and urinary cancer. Other preferred
					indications include benign dysproliferative disorders and
					pre-neoplastic conditions, such as, for example,
					hyperplasia, metaplasia, and/or dysplasia. A highly
					preferred indication is infection (e.g., tuberculosis,
					infections associated with granulomatous disease, and
					osteoporosis, and/or an infectious disease as described
					below under "Infectious Disease"). A highly preferred
					indication is AIDS. Additional highly preferred
					indications include suppression of immune reactions to
-					transplanted organs and/or tissues, uveitis, psoriasis, and
					tropical spastic paraparesis. Preferred indications
					include blood disorders (e.g., as described below under
					"Immune Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications also
					include anemia, pancytopenia, leukopenia,
					thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, granulomatous disease,
					inflammatory bowel disease, sepsis, neutropenia,
					neutrophilia, hemophilia, hypercoagulation, diabetes
					mellitus, endocarditis, meningitis, Lyme Disease, asthma
					and allergy.
219	HKAFF50	733	Upregulation of CD69	CD69 FMAT. CD69 is an activation	A highly preferred embodiment of the invention
			and activation of T cells	marker that is expressed on activated T	includes a method for activating T cells. An alternative
				cells, B cells, and NK cells. CD69 is not	highly preferred embodiment of the invention includes a

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expressed on resting T cells, B cells, or	method for inhibiting the activation of and/or inactivating
NK cells. CD69 has been found to be	T cells. A highly preferred embodiment of the
associated with inflammation. Assays for	n ii.
immunomodulatory proteins expressed in	alternative highly preferred embodiment of the invention
T cells, B cells, and leukocytes are well	includes a method for inhibiting the activation of and/or
known in the art and may be used or	inactivating B cells. A highly preferred embodiment
routinely modified to assess the ability of	of the invention includes a method for activating NK cells.
polypeptides of the invention (including	An alternative highly preferred embodiment of the
 antibodies and agonists or antagonists of	invention includes a method for inhibiting activation of
the invention) to modulate the activation of	and/or inactivation NK cells. Highly preferred
T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory
mediated immunity. Exemplary assays	disorders (e.g., as described below under "Immune
that test for immunomodulatory proteins	Activity"). Preferred indications include blood
evaluate the upregulation of cell surface	disorders (e.g., as described below under "Immune
markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
 immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,

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				recentor and CD3 CD4 or CD8 These	feukcinia, iyinpholila, ahwol as described below under "Hymerproliferative Disorders"). Preferred indications
				cells mediate humoral or cell-mediated	include neoplasms, such as, for example, leukemia,
				immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
				enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
				immunomodulatory factors.	Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
000	26240711	7.00			example, nyperplasia, metapiasia, and/or dyspiasia.
077	HKGBF25	/34	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		-	in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
		·· =		activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
		•		85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,

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			,	with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
221	HKIXC44	735	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-56 (1996); and, Misorlico S, et al., Incention of the invention of insulin Shimizu, H., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-56 (1996); and, Misorlico S, et al., Incention of the invention o	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious Diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include belosity. Additional highly preferred indications include belosity.

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highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for activation B cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating B cells. A highly preferred embodiment of the invention includes a method for inhibiting activation of and/or inactivation NK cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting activation of and/or inactivation NK cells. Highly preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity"). Preferred indications include blood disorders (e.g., as described below under "Immune".
Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface
	Upregulation of T cells and activation of T cells
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				morbare ench as CDKO and the nationalian	Anticity," "Dland Dalatad Diamban" and lan
				of T cells. Such assays that may be used	"Cardiouscular Disorders" Linkly preferred indications
				or routinely modified to test	cardiovascutat Disolucis). Luginiy preferred murcanolis include antoimmine diseases (e.g., rhenmatoid arthritis
				immunomodulatory activity of	systemic lupus erythematosis, multiple solerosis and/or as
-				polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
				antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
	-			approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
				(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
_				Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
				are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
				entirety. Human T cells that may be used	transplanted organs and tissues, hemophilia,
				according to these assays may be isolated	hypercoagulation, diabetes mellitus, endocarditis,
				using techniques disclosed herein or	meningitis, Lyme Disease, inflammation and
				otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
				are primary human lymphocytes that	Preferred indications also include neoplastic diseases (e.g.,
				mature in the thymus and express a T Cell	leukemia, lymphoma, and/or as described below under
				receptor and CD3, CD4, or CD8. These	"Hyperproliferative Disorders"). Preferred indications
				cells mediate humoral or cell-mediated	include neoplasms, such as, for example, leukemia,
				immunity and may be preactivated to	lymphoma, and prostate, breast, lung, colon, pancreatic,
				enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
				immunomodulatory factors.	Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
					example, hyperplasia, metaplasia, and/or dysplasia.
223	HKMLM95	737		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	inclu
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				1gG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune

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inaciophage achvallon; and increases	Activity, Blood-Kelated Disorders, and/or
MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
helper cell functions are well known in the	Highly preferred indications include autoimmune disease
art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
 invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
inflammatory activities, modulate TH2	indications include inflammation and inflammatory
helper cell function, and/or mediate	disorders. Additional preferred indications include
humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
polypeptides of the invention (including	include benign dysproliferative disorders and pre-
antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
of each of which are herein incorporated	
by reference in its entirety. Human T cells	
that may be used according to these assays	
may be isolated using techniques disclosed	

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			herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors	
224 HKTAB41	738	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic retinopathy, kidney diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications associated highly preferred indications as acciated highly preferred indications as ociated
			of each of which is herein incorporated by reference in its entirety. Pancreatic cells	with insulin resistance.

	S, agonists, or prevention, allergy,
	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.
these assays ough the y generated. I may be include adherent rom Syrian with SV40. d receptors. I is agon and 1777 hem. J. 219: Natl. Acad.	d d d d d d d d d d d d d d d d d d d
labele (e.g., throad be routinel; reatic cells that reatic cells that to these assays HITT15 are an established fls transformed ess glucagon, d glucocorticoi; insulin, which ucose and gluc matostatin or ATTC# CRLAShcroft. Biocite et al. Proc. 139-4343, 1981	or example kin the MAP kinas IAK, and ERK, and ERK and may be us and may be used to assess the invention (igonists or antage promote or inhoron in immune applary assays from including antil including an
that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation, and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, et al., J Immunol, et al., J Biol Chem, 275(46):35857-35862
	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).
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				(2000), the contents of each of which are herein incorporated by reference in its	
				entirety. Exemplary immune cells (for	
				example, 1-cells) that may be used	
	-			according to these assays include the mouse CTLL cell line.	
226	HLDCA54	740	Production of RANTES	RANTES FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that induce	includes a method for stimulating RANTES production.
				chemotaxis of T cells, monocytes, and	An alternative highly preferred embodiment of the
				eosinophils are well known in the art and	invention includes a method for inhibiting (e.g., reducing)
				may be used or routinely modified to	RANTES production. A highly preferred indication is
				assess the ability of polypeptides of the	infection (e.g., an infectious disease as described below
				invention (including antibodies and	under "Infectious Disease"). A most highly preferred
				agonists or antagonists of the invention) to	indication includes AIDS and/or the prevention or
				mediate immunomodulation, induce	reduction of HIV infection. Additional highly preferred
	٩			chemotaxis, and/or mediate humoral or	indication includes immune disorders, for example,
				cell-mediated immunity. Exemplary	inflammation and inflammatory disorders. Preferred
				assays that test for immunomodulatory	indications include blood disorders (e.g., as described
				proteins evaluate the production of	below under "Immune Activity", "Blood-Related
				cytokines, such as RANTES, and the	Disorders", and/or "Cardiovascular Disorders"). Highly
				induction of chemotactic responses in	preferred indications include autoimmune diseases (e.g.,
				immune cells. Such assays that may be	rheumatoid arthritis, systemic lupus erythematosis,
				used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications also include anemia, pancytopenia,
				antibodies and agonists or antagonists of	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				the invention) include the assays disclosed	lymphocytic anemia (ALL), plasmacytomas, multiple
				in Miraglia et al., J Biomolecular	myeloma, Burkitt's lymphoma, arthritis, asthma,
				Screening 4:193-204 (1999); Rowland et	granulomatous disease, inflammatory bowel disease,
				al., "Lymphocytes: a practical approach"	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				Chapter 6:138-160 (2000): Cocchi et al.,	immune reactions to transplanted organs and tissues,
		****		Science 270(5243):1811-1815 (1995); and	hemophilia, hypercoagulation, diabetes mellitus,
		· · · · · ·		Robinson et al., Clin Exp Immunol	endocarditis, meningitis, Lyme Disease, asthma, and
				101(3):398-407 (1995), the contents of	allergy. Highly preferred indications also include
				each of which are herein incorporated by	neoplastic diseases (e.g., leukemia, lymphoma, and/or as
				reference in its entirety. Human immune	described below under "Hyperproliferative Disorders").
				cells that may be used according to these	Highly preferred indications include neoplasms, such as,

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			assays may be isolated using techniques disclosed herein or otherwise known in the	for example, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and
			art.	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
227 HLDQU79	79 741	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
		and proliferation of	proliteration of cells in vitro are well-	An additional highly preferred indication is a complication
		pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
	••••		polypeptides of the invention (including antibodies and agonists of antibodies of	nephropathy and/or other diseases and disorders as
			the invention) to remiste vishility and	nestroct in the average disorder and nerve domester of the for
			nroliferation of pancreatic heta cells. For	diabetic neuronathy) blood vessel blockage heart disease
			example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
			cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion.
			viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
			quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
· · ·			signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
	·· ···		active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
			used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
			regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
			pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
			invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
	-		agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
			include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
			BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
-8			(2001); Huotari MA, et al., Endocrinology,	tunne
			139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
			Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
			(1998), the contents of each of which is	obesity. Additional highly preferred indications include
			herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
			entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
			according to these assays are publicly	with insulin resistance.
			available (e.g., through the ATCC) and/or	
			may be routinely generated. Exemplary	
			pancreatic cells that may be used	

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				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
		-		X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
\dashv				Endocrinology 1992 130:167.	
227	нгроп79	741	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
	_			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
	_			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
			-	incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred

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				2 dependent suspension culture of T cells with cytotoxic activity.	indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
228	HLDRT09	742	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred

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HLHAP05 743 Production of MIP1alpha	the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity. MIP-Lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein I alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention of chemotaxis activity of	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Infectious Disease"). Highly preferred indications and include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AlDS, granulomatous disease, inflammatory bowel disease,
	agonists or antagonists of the invention)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues.

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				promoter element activity (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
				the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci	Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuvtren's
				U.S.A., 97(8):3948-53 (2000); Roder, K.,	contracture). An additional highly preferred
				et al., Eur J Blochem, 200(3):/43-51 (1999); Oskouian B, et al., Biochem J, 317	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include
				(Pt 1):257-65 (1996); Berger, et al., Gene	weight loss or alternatively, weight gain. Aditional
				00:1-10 (1988); and, Cullen, B., et al., Methods in Fravmol 216:362–368 (1002)	highly preferred indications are complications associated
				the contents of each of which is herein	WITH THORITIN LOSISIANIOC.
				incorporated by reference in its entirety.	
				Hepatocytes that may be used according to	-
				these assays, such as H4IIE cells, are	
				publicly available (e.g., through the	
	_			ATCC) and/or may be routinely generated.	
				Exemplary hepatocytes that may be used	
				according to these assays include rat liver	
				hepatoma cell line(s) inducible with	
				glucocorticoids, insulin, or cAMP	
				derivatives.	
230	HLHCS23	744	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
		•	and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
			pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
				routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
				proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
				example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
***				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,

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			regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
			pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
			invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
			agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
			include assays disclosed in: Ohtani KI, et	diseases and disorders as described in the "Infectious
			al., Endocrinology, 139(1):172-8 (1998);	Diseases" section below, especially of the urinary tract and
			Krautheim A, et al, Exp Clin Endocrinol	skin), carpal tunnel syndrome and Dupuytren's
			Diabetes, 107 (1):29-34 (1999), the	contracture). An additional highly preferred
			contents of each of which is herein	indication is obesity and/or complications associated with
			incorporated by reference in its entirety.	obesity. Additional highly preferred indications include
			Pancreatic cells that may be used	weight loss or alternatively, weight gain. Aditional
			according to these assays are publicly	highly preferred indications are complications associated
			available (e.g., through the ATCC) and/or	with insulin resistance.
			may be routinely generated. Exemplary	
-			pancreatic cells that may be used	
			according to these assays include HITT15	
			Cells. HITT15 are an adherent epithelial	
			cell line established from Syrian hamster	
			islet cells transformed with SV40. These	
			cells express glucagon, somatostatin, and	
			glucocorticoid receptors. The cells secrete	
			insulin, which is stimulated by glucose and	
			glucagon and suppressed by somatostatin	
	-		or glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
			Sci. USA 78: 4339-4343, 1981.	
230 HLHCS23	744	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
-			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
			growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple

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				transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and	sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.
				agonists or antagonists of the invention) include assays disclosed in Berger et al.,	include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis.
	,			Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992):	An additional highly preferred indication is sepsis. Highly preferred indications include neonlastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				65:0342-0340 (1986); and black et al., Virus Genes 12(2):105-117 (1997), the	under Thyperprolliterative Disorders). Additionally, highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
20102				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicity available (e.g., through the ATCC). Exemplary mouse T cells that	stomach, orain, liver and urinary cancer. Uther preferred indications include benion dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is micchon (c.g., an infectious disease as described octow under "Infectious Disease").
230	HLHCS23	744	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
					invention includes a method for inhibiting the production
					of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or

infections, tuberculosis, infections associated with chronic immunodeficiency (e.g., as described below), boosting a T brain, liver and urinary cancer. Other preferred indications neutrophilia, psoriasis, suppression of immune reactions to Highly preferred indications include autoimmune disease cell-mediated immune response, and suppressing a T cellthrombocytopenia, Hodgkin's disease, acute lymphocytic disease, inflammatory bowel disease, sepsis, neutropenia, (e.g., rheumatoid arthritis, systemic lupus erythematosis, mediated immune response. Additional highly preferred example, leukemia, lymphoma, melanoma, and prostate, neoplastic conditions, such as, for example, hyperplasia, lymphoma, melanoma, and/or as described below under indications include neoplasms and cancers, such as, for and/or as described below under "Infectious Disease"), indications include neoplastic diseases (e.g., leukemia, 'Cardiovascular Disorders"), and infection (e.g., viral Preferred indications granulomatosus disease and malignant osteoporosis, breast, lung, colon, pancreatic, esophageal, stomach, Burkitt's lymphoma, arthritis, AIDS, granulomatous disorders. Additional preferred indications include indications include inflammation and inflammatory anemia (ALL), plasmacytomas, multiple myeloma, "Hyperproliferative Disorders"). Highly preferred include benign dysproliferative disorders and preidiopathic pulmonary fibrosis. Highly preferred hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. multiple sclerosis and/or as described below), transplanted organs and tissues, hemophilia, include anemia, pancytopenia, leukopenia, metaplasia, and/or dysplasia. (Oxford) 38(3):214-20 (1999), the contents agonists or antagonists of the invention) to production of cytokines, such as Interferon helper cell functions are well known in the Chapter 6:138-160 (2000); Gonzalez et al., T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 by reference in its entirety. Human T cells may be isolated using techniques disclosed to assess the ability of polypeptides of the the invention) include the assays disclosed Billiau et al., Ann NY Acad Sci 856:22-32 art and may be used or routinely modified that may be used according to these assays immunomodulatory proteins produced by (1998); Boehm et al., Annu Rev Immunol immunomodulatory proteins evaluate the Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" antibodies and agonists or antagonists of polypeptides of the invention (including of each of which are herein incorporated 15:749-795 (1997), and Rheumatology inflammatory activities, modulate TH2 gamma (IFNg), and the activation of T cells. Such assays that may be used or mediate immunomodulation, regulate J Clin Lab Anal 8(5):225-233 (1995); helper cell function, and/or mediate humoral or cell-mediated immunity. herein or otherwise known in the art. invention (including antibodies and in Miraglia et al., J Biomolecular immunomodulatory activity of Exemplary assays that test for MHC expression. Assays for routinely modified to test

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				Uramon T calle and maintains breases	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
+				immunomodulatory factors.	
231	HLIBO72	745	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
-			-	the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic

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232	HLICE88	746	Activation of transcription through serum response element in immune cells (such	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the	anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays	increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, braait, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example,

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			2 dependent suspension culture of T cells with cytotoxic activity.	indications include anemia, pancytopenia, Proteined indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
232 HLICE88	746	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1065); and Miradia S. at al. Journal of	A highly preferred indication is diabetes mellitus. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious diseases and disorders as described in the "Infectious diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred

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				Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
233	HLICO10	747	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally

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HLJBS28	748	Activation of transcription through serum response element in immune cells (such as T-cells).	Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity. Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectious Disease, cardiac reperfusion includes a method for stimulating (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies
			used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and accounts or attaconies of the invention)	(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications
		3	agonists of antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.

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				Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic
		-			anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, ALDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and ussues, nemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication
2,56	2011107	Ç.			is infection (e.g., an infectious disease as described below under "Infectious Disease").
733	HLMBW89	749	Upregulation of CD154 and activation of T cells	CD154 FMAT. CD154 (a.k.a., CD40L) expression is induced following activation of T cells. Internaction between CD154	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes
			-	and CD40 on B cells is required for correct antibody class switching and germinal	method for inhibiting the activation of and/or inactivating T cells. Highly preferred indications include blood
				Center formation. Mutations in CD134 are linked to immunodeficiencies and increased encountiility to infections	Activity, "Blood-Related Disorders", and/or
				Assays for immunomodulatory proteins	Caludovascular Disorders), and infection (e.g., as described below under "Infectious Disease"). Highly
				important for antibody class switching and TH1 function and expressed on activated T	preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis.
				helper lymphocytes are well known in the	multiple sclerosis and/or as described below) and
				to assess the ability of polypeptides of the	infinite indications (e.g., ALDS). Preferred indications include boosting a T cell-mediated immune response, and

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				invention (including antibodies and	alternatively conneccing a Tool mediated immine
				agonists or antagonists of the invention) to	response Preferred indications include neonlystic
		-		modulate the activation of T cells,	ы
				modulate antibody class switching,	below under "Hyperproliferative Disorders"). Highly
				mediate TH1 function, and/or mediate	preferred indications include neoplasms, such as, for
				humoral or cell-mediated immunity.	example, leukemia, lymphoma, and prostate, breast, lung,
				Exemplary assays that test for	colon, pancreatic, esophageal, stomach, brain, liver and
				immunomodulatory proteins evaluate the	urinary cancer. Other preferred indications include benign
				upregulation of cell surface markers, such	dysproliferative disorders and pre-neoplastic conditions,
				as CD154, and the activation of T cells.	such as, for example, hyperplasia, metaplasia, and/or
				Such assays that may be used or routinely	dysplasia. Preferred indications also include anemia,
				modified to test immunomodulatory	pancytopenia, leukopenia, thrombocytopenia, leukemias,
				activity of polypeptides of the invention	Hodgkin's disease, acute lymphocytic anemia (ALL),
				(including antibodies and agonists or	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				antagonists of the invention) include, for	arthritis, AIDS, granulomatous disease, inflammatory
				example, the assays disclosed in Miraglia	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis.
				et al., J Biomolecular Screening 4:193-204	immune reactions to transplanted organs and tissues.
				(1999); Rowland et al., "Lymphocytes: a	hemophilia, hypercoagulation, diabetes mellitus.
				practical approach" Chapter 6:138-160	endocarditis, meningitis, Lyme Disease, inflammation and
				(2000); Mackey et al., J Leukoc Biol	inflammatory disorders, and asthma and allergy.
				63(4):418:428 (1998); and Skov et al.,	
				164(7):3500-3505 (2000), the contents of	
				each of which are herein incorporated by	
				reference in its entirety. Human T cells	
				that may be used according to these assays	
				may be isolated using techniques disclosed	
				herein or otherwise known in the art.	
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
236	HLMGP50	750	Upregulation of HLA-	HLA-DR FMAT. MHC class II is essential	Highly preferred indications include blood disorders
			DR and activation of T	for correct presentation of antigen to CD4+	(e.g., as described below under "Immune Activity",
			cells	T cells. Deregulation of MHC class II has	"Blood-Related Disorders", and/or "Cardiovascular

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	been associated with autoimmune diseases	Disorders"). Highly preferred indications include
	(e.g., diabetes, rneumatoid arthritis, systemic lupus erythematosis, and multiple	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described
	sclerosis). Assays for immunomodulatory	below) and immunodeficiencies (e.g., as described below),
	proteins expressed on MHC class II	boosting a T cell-mediated immune response, and
	expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
	cells are well known in the art and may be	response. A highly preferred indication is diabetes
	used or routinely modified to assess the	mellitus. An additional highly preferred indication
	ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
	(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
	antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
	the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
	humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
	Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
	immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
	upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
-	such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
	activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
	be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
	immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
	polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
	antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
	the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
	assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
	Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
	Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
	approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
	Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
	89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
	Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
	Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
	117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
	Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
	the contents of each of which are herein	are complications associated with insulin resistance.
	incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
	Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
	to these assays may be isolated using	dystrophy, and/or as described herein.

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			techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	additional preferred indication is infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and allergy.
237 HLMJB64	751	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred

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			66:1-10 (1988): Cullen and Malm.	indications include neonlasms and cancers such as
			Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon.
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
			Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
-			Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
			4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
			Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
			cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
			assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
			the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
			may be used according to these assays	meningitis, and Lyme Disease.
			include the CTLL cell line, which is an IL-	
			2 dependent suspension-culture cell line	
			with cytotoxic activity.	
237 HLMJB64	751	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
		transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
		cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
		element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
		cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
			antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
			the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
			regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
			modulate expression of genes involved in a	described below), boosting a T cell-mediated immune
			wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
-			assays for transcription through the cAMP	response. Additional preferred indications include
			response element that may be used or	inflammation and inflammatory disorders. Highly
			routinely modified to test cAMP-response	હું
-			element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
			invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
			agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
			include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
			Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
			Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary

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				85.6342-6346 (1988): Black et al Virus	concer Other preferred indications include henion
				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions.
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia,
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
		·		according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the	transplanted organs and tissues, hemophilia,
				CTLL cell line, which is a suspension	hypercoagulation, diabetes mellitus, endocarditis,
				culture of IL-2 dependent cytotoxic T cells.	meningitis, Lyme Disease, and asthma and allergy.
237 HL	HLMJB64	751	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
			-	85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,

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				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
	***			are herein incorporated by reterence in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
237	HLMJB64	751	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
		_		cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred

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indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred inflammatory disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. An additional highly preferred indication includes infection e.g., AIDS, and/or as described below under "Infectious
the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:632-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
	751
	HLMJB64
	237

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238 HIWAGO	632		al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma, lymphoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", ethrombocytopenia, Hodgkin's disease, acute lymphocytic anemia, pancytopenia, leukopenia, henophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
	76/	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the

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assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
invention (including antibodies and	differentiation. An alternative highly preferred
agonists or antagonists of the invention) to	embodiment of the invention includes a method for
promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 313-L1 cells. 373-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
1s a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the

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indications include blood disorders (e.g., neutropenia (and indications include asthma. Highly preferred indications "Cardiovascular Disorders"). Highly preferred indications leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and psoriasis, hemophilia, hypercoagulation, diabetes mellitus, and/or as described below) and immunodeficiencies (e.g., progenitor cells. Preferred indications include boosting leukopenia, thrombocytopenia, acute lymphocytic anemia lung, colon, pancreatic, esophageal, stomach, brain, liver arthritis, systemic lupus erythematosis, multiple sclerosis conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications include: suppression of immune reactions to transplanted organs and tissues (e.g., bone marrow transplant); accelerating and urinary cancer. Other preferred indications include include neoplastic diseases (e.g., leukemia (e.g., acute a T cell-mediated immune response, and alternatively, leukemia, lymphoma, melanoma, and prostate, breast, (ALL), plasmacytomas, multiple myeloma, Burkitt's Hodgkin's disease), and/or as described below under patients), and/or as described below under "Immune benign dysproliferative disorders and pre-neoplastic also include autoimmune diseases (e.g., rheumatoid indications include neoplasms and cancers, such as, Preferred indications include anemia, pancytopenia, endocarditis, meningitis, Lyme Disease, and allergy. the prevention of neutropenia (e.g., in HIV infected lymphoma, arthritis, AIDS, granulomatous disease, "Hyperproliferative Disorders"). Highly preferred as described below). Additional highly preferred inflammatory bowel disease, sepsis, neutrophilia, myeloid recovery; and mobilizing hematopoietic lymphoblastic leukemia, and acute myelogenous suppressing a T cell-mediated immune response. Activity", "Blood-Related Disorders", and/or agonists or antagonists of the invention) to mediate immunomodulation and modulate production of cytokines, such as GM-CSF, known in the art. Natural killer (NK) cells cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of eukocytes. Exemplary assays that test for assays are publicly available (e.g., through and the activation of T cells. Such assays the invention) include the assays disclosed Chapter 6:138-160 (2000); and Ye et al., J Leukoc Biol (58(2):225-233, the contents that may be used or routinely modified to immunomodulatory proteins evaluate the an important role in the differentiation of Screening 4:193-204 (1999); Rowland et by reference in its entirety. Natural killer increases antigen presentation. GM-CSF cytokine. Assays for immunomodulatory antibodies and agonists or antagonists of cells that may be used according to these are large granular lymphocytes that have of each of which are herein incorporated polypeptides of the invention (including al., "Lymphocytes: a practical approach" techniques disclosed herein or otherwise proteins that promote the production of assess the ability of polypeptides of the GM-CSF are well known in the art and is considered to be a proinflammatory may be used or routinely modified to the ATCC) or may be isolated using invention (including antibodies and est immunomodulatory activity of dendritic cells and monocytes, and in Miraglia et al., J Biomolecular the growth and differentiation of

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				tumor cells and also recognize antibody	
				bound on target cells, via NK Fc receptors,	
240	H OCI 64	754	IIImmuniption of CD60	CDCO TAKAT CDCO	
) †	וווילכנים	+C/	Opregulation of CD69	CD69 FIMAL. CD69 is an activation	A highly preferred embodiment of the invention
			and activation of T cells	marker that is expressed on activated T	includes a method for activating T cells. An alternative
_	<u>.</u>			cells, B cells, and NK cells. CD69 is not	highly preferred embodiment of the invention includes a
				expressed on resting T cells, B cells, or	method for inhibiting the activation of and/or inactivating
				NK cells. CD69 has been found to be	T cells. A highly preferred embodiment of the
				associated with inflammation. Assays for	invention includes a method for activation B cells. An
				immunomodulatory proteins expressed in	alternative highly preferred embodiment of the invention
		*		T cells, B cells, and leukocytes are well	includes a method for inhibiting the activation of and/or
				known in the art and may be used or	inactivating B cells. A highly preferred embodiment
				routinely modified to assess the ability of	of the invention includes a method for activating NK cells.
				polypeptides of the invention (including	An alternative highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for inhibiting activation of
				the invention) to modulate the activation of	and/or inactivation NK cells. Highly preferred
				T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory
				mediated immunity. Exemplary assays	disorders (e.g., as described below under "Immune
				that test for immunomodulatory proteins	Activity"). Preferred indications include blood
				evaluate the upregulation of cell surface	60
				markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
				of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
				or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
				polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
		•		antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
		•		approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
		···		(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,

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			are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningits I vme Disease inflammation and
			otherwise known in the art. Human T cells	inflammatory disorders, asthma, and allergies.
			are primary numan lymphocytes that mature in the thymus and express a T Cell	Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under
			receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated	"Hyperproliferative Disorders"). Preferred indications
			immunity and may be preactivated to	Include heoptabilis, such as, for example, feukenna, lymphoma, and prostate, breast, lung, colon, pancreatic,
			enhance responsiveness to	esophageal, stomach, brain, liver and urinary cancer.
-			immunomodulatory factors.	Other preferred indications include benign dysproliferative
$\neg \vdash$				usoricets and pre-neoptastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
241 HLQCX36	755	Activation of Skeletal	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		Mucle Cell PI3 Kinase	an GSK-3 kinase assay, for PI3 kinase	includes a method for increasing muscle cell survival An
		Signalling Pathway	signal transduction that regulate glucose	alternative highly preferred embodiment of the invention
-			metabolism and cell survivial are well-	includes a method for decreasing muscle cell survival.
			known in the art and may be used or	A preferred embodiment of the invention includes a
			routinely modified to assess the ability of	method for stimulating muscle cell proliferation. In a
			polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is
			antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
	-		the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
			glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
			Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
			that may be used or routinely modified to	of the invention includes a method for stimulating muscle
			test F13 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
			portpetities of the invention (including anti-hodies and agonists of anti-hodies of	muscle cell differentiation is stimulated. An alternative
			the invention) include assays disclosed in	method for inhihiting muscle cell differentiation. In a
			Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment skeletal muscle cell differentiation is
			1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
			49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
			Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
			contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
			incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
			Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity

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according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
available (e.g., through the ATCC).	described below under "Immune Activity",
Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
cells. L6 is an adherent rat myoblast cell	under "Immune Activity"), and infection (e.g., as
line, isolated from primary cultures of rat	described below under "Infectious Disease"). A
thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus.
multinucleated myotubes and striated	additional highly preferred indication is a complication
fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g., due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infections (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below, especially of the urinary tract and
	skin), carpal tunnel syndrome and Dupuytren's
	contracture). An additional highly preferred indication
	is obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additonal highly preferred
	indications are disorders of the musculoskeletal system
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred

Designation.

242	HLWAF06	756	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia. A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic Highly preferred indications also include neoplastic
				Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature	diseases (e.g., iipomas, iiposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart
					disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity

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be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional night) preferred indication is a complication
include 313-L1 cells. 313-L1 18 an	associated with diabetes (e.g., diabetic retinopatity,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
 is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
 -	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
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	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and

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breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely
	Production of ICAM-1	Production of ICAM-1
	757	758
	HLWAU42	HLWAU42
	243	244

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				modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC)	
245	HLWAV47	759	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast luno colon paperearic escorbageal

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assays the A' may b includ 2 depp with c With c With C IL-6 F and ha partici and in role in cytoto of IL-6 diseass chroni Assays differe a large expres cytoki are we or rout of poly antibo the inv		stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include below under "Inmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response and alternatively suppressing a B cell-mediated immune response and inflammatory disorders. Additional highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include inflammatory alicetions include indications include indicatio
i	Production of IL-6	assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL. 2 dependent suspension culture of T cells with cytotoxic activity. L-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention and differentiation and inferentiation and inferentiation and inferentiation and inferentiation and

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				Exemplary assays that test for	neoplastic diseases (e.g. myeloma nlasmacytoma
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
			•	modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
	•			(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
247	HLWCN37	761		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").

brain, liver and urinary cancer. Other preferred indications neutrophilia, psoriasis, suppression of immune reactions to immunodeficiency (e.g., as described below), boosting a T thrombocytopenia, Hodgkin's disease, acute lymphocytic disease, inflammatory bowel disease, sepsis, neutropenia, Highly preferred indications include autoimmune disease cell-mediated immune response, and suppressing a T cell (e.g., rheumatoid arthritis, systemic lupus erythematosis, mediated immune response. Additional highly preferred neoplastic conditions, such as, for example, hyperplasia, example, leukemia, lymphoma, melanoma, and prostate, lymphoma, melanoma, and/or as described below under indications include neoplasms and cancers, such as, for indications include neoplastic diseases (e.g., leukemia, metaplasia, and/or dysplasia. Preferred indications breast, lung, colon, pancreatic, esophageal, stomach, Burkitt's lymphoma, arthritis, AIDS, granulomatous indications include inflammation and inflammatory disorders. Additional preferred indications include anemia (ALL), plasmacytomas, multiple myeloma, idiopathic pulmonary fibrosis. Highly preferred "Hyperproliferative Disorders"). Highly preferred include benign dysproliferative disorders and prehypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. multiple sclerosis and/or as described below). transplanted organs and tissues, hemophilia, include anemia, pancytopenia, leukopenia, (Oxford) 38(3):214-20 (1999), the contents Chapter 6:138-160 (2000); Gonzalez et al., agonists or antagonists of the invention) to helper cell functions are well known in the production of cytokines, such as Interferon by reference in its entirety. Human T cells may be isolated using techniques disclosed Billiau et al., Ann NY Acad Sci 856:22-32 that may be used according to these assays ymphocytes that mature in the thymus and to assess the ability of polypeptides of the the invention) include the assays disclosed art and may be used or routinely modified (1998); Boehm et al., Annu Rev Immunol immunomodulatory proteins evaluate the Screening 4:193-204 (1999); Rowland et express a T Cell receptor and CD3, CD4, polypeptides of the invention (including antibodies and agonists or antagonists of al., "Lymphocytes: a practical approach" of each of which are herein incorporated or CD8. These cells mediate humoral or gamma (IFNg), and the activation of T 15:749-795 (1997), and Rheumatology inflammatory activities, modulate TH2 cells. Such assays that may be used or mediate immunomodulation, regulate J Clin Lab Anal 8(5):225-233 (1995); herein or otherwise known in the art. invention (including antibodies and helper cell function, and/or mediate humoral or cell-mediated immunity. Human T cells are primary human in Miraglia et al., J Biomolecular immunomodulatory activity of Exemplary assays that test for routinely modified to test

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				of mediated imministry and mary ha	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
248	HLWDB73	762	Activation of Skeletal	Kinase assay. Kinase assays, for examplek	Highly preferred indications include endocrine
			Muscle Cell ERK	Elk-1 kinase assays, for ERK signal	disorders (e.g., as described below under "Endocrine
			Signalling Pathway	transduction that regulate cell proliferation	Disorders") and disorders of the musculoskeletal system.
				or differentiation are well known in the art	Preferred indications include neoplastic diseases (e.g., as
······································				and may be used or routinely modified to	described below under "Hyperproliferative Disorders"),
				assess the ability of polypeptides of the	blood disorders (e.g., as described below under "Immune
				invention (including antibodies and	Activity", "Cardiovascular Disorders", and/or "Blood-
		• • • •		agonists or antagonists of the invention) to	Related Disorders"), immune disorders (e.g., as described
				promote or inhibit cell proliferation,	below under "Immune Activity"), neural disorders (e.g., as
				activation, and differentiation. Exemplary	described below under "Neural Activity and Neurological
				assays for ERK kinase activity that may be	Diseases"), and infection (e.g., as described below under
				used or routinely modified to test ERK	"Infectious Disease"). A highly preferred indication
				kinase-induced activity of polypeptides of	
				the invention (including antibodies and	indication is a complication associated with diabetes (e.g.,
				agonists or antagonists of the invention)	diabetic retinopathy, diabetic nephropathy, kidney disease
				include the assays disclosed in Forrer et	(e.g., renal failure, nephropathy and/or other diseases and
				al., Biol Chem 379(8-9):1101-1110	disorders as described in the "Renal Disorders" section
				(1998); Le Marchand-Brustel Y, Exp Clin	below), diabetic neuropathy, nerve disease and nerve
				Endocrinol Diabetes 107(2):126-132	damage (e.g., due to diabetic neuropathy), blood vessel
				(1999); Kyriakis JM, Biochem Soc Symp	blockage, heart disease, stroke, impotence (e.g., due to
				64:29-48 (1999); Chang and Karin, Nature	diabetic neuropathy or blood vessel blockage), seizures,
				410(6824):37-40 (2001); and Cobb MH,	mental confusion, drowsiness, nonketotic hyperglycemic-
				Prog Biophys Mol Biol 71(3-4):479-500	hyperosmolar coma, cardiovascular disease (e.g., heart
				(1999); the contents of each of which are	disease, atherosclerosis, microvascular disease,
				herein incorporated by reference in its	hypertension, stroke, and other diseases and disorders as
				entirety. Rat myoblast cells that may be	described in the "Cardiovascular Disorders" section
				used according to these assays are publicly	below), dyslipidemia, endocrine disorders (as described in
				available (e.g., through the ATCC).	the "Endocrine Disorders" section below), neuropathy,
				Exemplary rat myoblast cells that may be	vision impairment (e.g., diabetic retinopathy and
				used according to these assays include L6	blindness), ulcers and impaired wound healing, infection
				cells. L6 is an adherent rat myoblast cell	(e.g., infectious diseases and disorders as described in the
				line, isolated from primary cultures of rat	"Infectious Diseases" section below, especially of the
				thigh muscle, that fuses to form	urinary tract and skin), carpal tunnel syndrome and
				multinucleated myotubes and striated	Dupuytren's contracture). An additional highly

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	·			fibers after culture in differentiation media.	preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Highly preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hymeralasia metaplasia
249	HLYDF73	763	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment

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(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. d. Aditional highly preferred indications associated with insulin resistance. S. S	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lums erzyhematosis
antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for
	Activation of transcription through API response element in immune cells (such as T-cells).
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				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			•	85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
		• • •		Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
				Mouse T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
				to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
				through the ATCC). Exemplary mouse T	reactions to transplanted organs and tissues, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the HT2 cell line, which is	
_				an IL-2 dependent suspension culture cell	
				line that also responds to IL-4.	
251	HLYGB19	765	Activation of Skeletal	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Mucle Cell PI3 Kinase	an GSK-3 kinase assay, for PI3 kinase	includes a method for increasing muscle cell survival An
		•	Signalling Pathway	signal transduction that regulate glucose	alternative highly preferred embodiment of the invention
				metabolism and cell survivial are well-	includes a method for decreasing muscle cell survival.
				known in the art and may be used or	A preferred embodiment of the invention includes a
				routinely modified to assess the ability of	method for stimulating muscle cell proliferation. In a
				polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is
				antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
				the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
		•		glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
				Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
				that may be used or routinely modified to	of the invention includes a method for stimulating muscle
				test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal

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additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy,	multinucleated myotubes and striated fibers after culture in differentiation media.
described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An	line, isolated from primary cultures of rat thigh muscle, that fuses to form
Disorders"), immune disorders (e.g., as described below under "Immune Activity"), and infection (e.g., as	used according to these assays include L6 cells. L6 is an adherent rat myoblast cell
"Cardiovascular Disorders", and/or "Blood-Related	Exemplary rat myoblast cells that may be
and Neurological Diseases"), blood disorders (e.g., as described below under "Immune Activity".	according to these assays are publicly available (e.g., through the ATCC).
as described below under "Endocrine Disorders"), neural disorders (e.g., as described below under "Neural Activity	incorporated by reference in its entirety. Rat myoblast cells that may be used
"Hyperproliferative Disorders"), endocrine disorders (e.g.,	contents of each of which are herein
of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under	49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the
inhibited. Highly preferred indications include disorders	1110 (1998); Nikoulina et al., Diabetes
method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is	the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-
muscle cell differentiation is stimulated. An alternative highly preferred embodiment of the invention includes a	polypeptides of the invention (including antibodies and agonists or antagonists of

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Total Digital and activation of CD152 PMAT. CD152 (a.k.a. CTLA-4) Total Digital and activation of CD152 may lead to byperpoliferation of CD152 may lead to impaired for the minitoration should not profession in the maintenance of T cells are well who may not the minitoration should for the immunomodulatory profession in the maintenance of T cells are well who may be a method for inhibiting preferred embodiment of the immunomodulatory profession in the maintenance of T cells are well who may be a method for inhibiting preferred embodiment of the majoritation and autoimmune diseases. Assays for the invention includes a method for inhibiting preferred embodiment of the invention includes a method for inhibiting preferred embodiment of the invention includes a method for inhibiting T cell immunoresponses. Sasays to CD8-1 cells are well known in the art and may be used to routinely modified to assess the ability of polypeptides of the profession includes a method for cativating T cell immunomodulatory proteins important in the major profession in the art and may be used to routinely modified to assess the ability of polypengias of the invention includes and profession in the art and manifessi
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				modulate the activation of T calls	innraccing of T call mediated immine reconces
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
		-		immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
_				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
		···-		Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
252	HLYGE16	992	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
				(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
		1	in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,

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		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to bind the	"Immune Activity", "Blood-Related Disorders", and/or
			serum response factor and modulate the	"Cardiovascular Disorders"), Highly preferred indications
			expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
			and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
			related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
			Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
			the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
-			modified to test SRE activity of the	immune response. Additional highly preferred indications
			polypeptides of the invention (including	include inflammation and inflammatory disorders, and
			antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
			the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
			Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
			and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
			368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
			Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
			Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
			3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
			12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
			of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
			reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
			be used according to these assays are	pre-neoplastic conditions, such as, for example,
			publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
			ATCC). Exemplary human T cells, such	indications include anemia, pancytopenia, leukopenia,
			as the MOLT4, that may be used according	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			to these assays are publicly available (e.g.,	anemia (ALL), plasmacytomas, multiple myeloma,
			through the ATCC).	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, neutropenia,
				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below under "Infectious Disease")
252 HLYGE16	992	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy. Another

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			transcription through	through the Signal Transducers and	highly preferred indication is asthma. Additional
			STAT6 response	Activators of Transcription (STAT6)	ons incl
		****	calle (euch of nothing)	response element are Well-Known in the art	inflammatory disorders. Preferred indications
			Cells (such as natural Liller cells)	and may be used of routinery modified to	"Transing Astivity," "Digg Beleast Diggs of Diggs and Control of the Control of t
			Aillet Calls).	assess the ability of polypeptities of the invention (including antibodies and	illilling Activity, Diood-Related Disorders, and/or "Cardiovascular Disorders") Preferred indications include
-:				agonists or antagonists of the invention) to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
		111		regulate STAT6 transcription factors and	lupus erythematosis, multiple sclerosis and/or as described
				modulate the expression of multiple genes.	below) and immunodeficiencies (e.g., as described below).
				Exemplary assays for transcription through	Preferred indications include neoplastic diseases (e.g.,
				the STAT6 response element that may be	leukemia, lymphoma, melanoma, and/or as described
				used or routinely modified to test STAT6	below under "Hyperproliferative Disorders"). Preferred
				response element activity of the	indications include neoplasms, such as, for example,
				polypeptides of the invention (including	leukemia, lymphoma, melanoma, and prostate, breast,
				antibodies and agonists or antagonists of	lung, colon, pancreatic, esophageal, stomach, brain, liver
				the invention) include assays disclosed in	and urinary cancer. Other preferred indications include
				Berger et al., Gene 66:1-10 (1998); Cullen	benign dysproliferative disorders and pre-neoplastic
				and Malm, Methods in Enzymol 216:362-	conditions, such as, for example, hyperplasia, metaplasia,
				368 (1992); Henthorn et al., Proc Natl	and/or dysplasia. Preferred indications include
				Acad Sci USA 85:6342-6346 (1988);	enia, leukop
		• • • • • • • • • • • • • • • • • • • •		Georas et al., Blood 92(12):4529-4538	Hodgkin's disease, acute lymphocytic anemia (ALL),
		-		(1998); Moffatt et al., Transplantation	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				69(7):1521-1523 (2000); Curiel et al., Eur	arthritis, AIDS, granulomatous disease, inflammatory
				J Immunol 27(8):1982-1987 (1997); and	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				Masuda et al., J Biol Chem	suppression of immune reactions to transplanted organs
		·		275(38):29331-29337 (2000), the contents	and tissues, hemophilia, hypercoagulation, diabetes
				of each of which are herein incorporated	mellitus, endocarditis, meningitis, and Lyme Disease.
	-			by reference in its entirety. T cells that	Additional preferred indications include infection (e.g., an
				may be used according to these assays are	infectious disease as described below under "Infectious
				publicly available (e.g., through the	Disease").
				ATCC). Exemplary rat natural killer cells	
				that may be used according to these assays	
				are publicly available (e.g., through the	
				ATCC).	
253	HLYGY91	167	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
				are well-known in the art and may be used	An additional highly preferred indication is a complication
				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,

	of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
	antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
	the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
	secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
	is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
	insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
	pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
-	glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
	proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
	key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
	assays that may be used or routinely	stroke, and other diseases and disorders as described in the
	modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
-	secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
	polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
	antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
	the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
	Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
	(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
	Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
	Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
	865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
	Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
	Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
	Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
	of each of which is herein incorporated by	with insulin resistance.
	reference in its entirety. Pancreatic cells	
	that may be used according to these assays	
	are publicly available (e.g., through the	
	ATCC) and/or may be routinely generated.	
	Exemplary pancreatic cells that may be	
	used according to these assays include	
	HITT15 Cells. HITT15 are an adherent	
	epithelial cell line established from Syrian	
	hamster islet cells transformed with SV40.	
	These cells express glucagon,	
	somatostatin, and glucocorticoid receptors.	
	The cells secrete insulin, which is	

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				ctimulated by almoste and almost and	
			-	summand by glacost and glacagon and	
				suppressed by somatostatin or	
				Before I and and Achande Biochem 1 210.	
				Neis Loid and Asherolt. Diochem. J. 219.	
				54/-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
254	HMCAZ04	892	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	ı.
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	orde
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy.

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		adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
		is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
		cells developed through clonal isolation	described in the "Kenal Disorders" section below), diabetic
		and under go a pre-adipocyte to adipose-	disheria mantanatha) blood manal blookees been diagon
		differentiation conditions known in the art	character incurvating), order vesses orderwage, incart disease, stroke importance (e.g. due to diabetic neuropathy or
			blood vessel blockage) seizures mental confusion
			drowsiness, nonketotic hymerolycemic-hymerosmolar
			coma, cardiovascular disease (e.g., heart disease.
			atherosclerosis, microvascular disease, hypertension.
			stroke, and other diseases and disorders as described in the
			"Cardiovascular Disorders" section below), dyslipidemia,
			endocrine disorders (as described in the "Endocrine
			Disorders" section below), neuropathy, vision impairment
			(e.g., diabetic retinopathy and blindness), ulcers and
			impaired wound healing, infection (e.g., infectious
	•		diseases and disorders as described in the "Infectious
			Diseases" section below (particularly of the urinary tract
			and skin). An additional highly preferred indication is
			obesity and/or complications associated with obesity.
			Additional highly preferred indications include weight loss
			or alternatively, weight gain. Additional highly
			ns are
			insulin resistance. Additional highly preferred
			indications are disorders of the musculoskeletal systems
-		¥	hies,
			described herein. Additional highly preferred
			indications include, hypertension, coronary artery disease,
			dyslipidemia, gallstones, osteoarthritis, degenerative
	-		arthritis, eating disorders, fibrosis, cachexia, and kidney
	•		diseases or disorders. Preferred indications include
			neoplasms and cancer, such as, lymphoma, leukemia and
			breast, colon, and kidney cancer. Additional preferred
			indications include melanoma, prostate, lung, pancreatic,
			esophageal, stomach, brain, liver, and urinary cancer.
			Highly preferred indications include lipomas and
			liposarcomas. Other preferred indications include benign

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					dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
230	10404704	072	A chimomist of A dimension	Vince agent Vince agent for eventle	dysplasia. A highly preferred embodiment of the invention
CC7	nimCA204	607	FRK Signaling	Milase assay: milase assays, for champic an Hlk-1 kinase assay for FRK signal	includes a method for stimulating adinocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			, minus	or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
_				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
•				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
***************************************				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
				cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic

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and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental contusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and
	breast, colon, and kidney cancer. Additional preferred
	indications include melanoma, prostate, lung, pancreatic,
	esophageal, stomach, brain, liver, and urinary cancer.
	Highly preferred indications include lipomas and
	liposarcomas. Other preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia.

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A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method preferred embodiment of the invention includes a method	alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart	disease, stroke, imported and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as	described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or
Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary	assays for EKK Kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64-20-48 (1900). Chang and Karin Nature	410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast	cells developed through clonal isolation and undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation conditions known in the art.
Activation of Adipocyte ERK Signaling Pathway			
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	-				drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious Diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
257	HMCAZ04	771	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation	dysplasia. A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the

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	or differentiation are well known in the art	invention includes a method for inhibiting adjunction
	and may be used or routinely modified to	nroliferation A highly preferred embodiment of the
	assess the ability of polypeptides of the	- 8
:	invention (including antibodies and	differentiation. An alternative highly preferred
	agonists or antagonists of the invention) to	embodiment of the invention includes a method for
	promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
	activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
	assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
	used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
	kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
	the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
	agonists or antagonists of the invention)	ırde
	include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
	al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
	(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
	that may be used according to these assays	additional highly preferred indication is a complication
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,

HMC	Activities of Adinocate	Activation of Adipocyte Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal incl Pathway transduction that regulate cell proliferation An or differentiation are well known in the art inverse and may be used or routinely modified to prolyaeses the ability of nolymentides of the inverse contraction or assess the ability of nolymentides of the inverse contraction.
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	and including antihodies and	differentiation. An alternative highly preferred
	of (notine of the distinct of the intention) to	
	agomets of antagomets of the invention to	
	promote or inhibit cell proliteration,	inhibiting adipocyte differentiation. A highly
	activation, and differentiation. Exemplary	
	assays for ERK kinase activity that may be	
	used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
	kinase-induced activity of polypeptides of	ion c
	the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
	agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
	include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
	al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
	(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	
	that may be used according to these assays	
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
-	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		Cardiovascular Disorders section below), dysnipidenna,

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ļ				endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment
				(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious
				diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract
				and skin). An additional highly preferred indication is
				opesity and/or complications associated with opesity. Additional highly preferred indications include weight loss
				or alternatively, weight gain. Additional highly
				ons are
				indications are disorders of the macon colorious
				including myopathies, muscular dystrophy, and/or as
				described herein. Additional highly preferred
				indications include, hypertension, coronary artery disease,
				dyslipidemia, gallstones, osteoarthritis, degenerative
				arthritis, eating disorders, fibrosis, cachexia, and kidney
				diseases or disorders. Preferred indications include
				neoplasms and cancer, such as, lymphoma, leukemia and
				breast, colon, and kidney cancer. Additional preferred
				indications include melanoma, prostate, lung, pancreatic,
				esophageal, stomach, brain, liver, and urinary cancer.
				Highly preferred indications include lipomas and
				liposarcomas. Other preferred indications include benign
				dysproliferative disorders and pre-neoplastic conditions,
				such as, for example, hyperplasia, metaplasia, and/or
259 HMCFH60	773	Activation of	Assays for the activation of transcrintion	Oyspiasia. Dreferred indications include neonlastic diseases (e.g.
) - -	transcription through	through the API response element are	as described below under "Hyperproliferative Disorders")
		AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
		in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
		as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
			antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
			the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
			other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
			uanscription unough the Art 1 response	multiple sciencis amund as described below) and

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				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
			-	assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
	•			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
- , .				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
259 HMG	НМСЕН60	773	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
	,		in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
	•			antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
_				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described

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			,	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
259	НМСРН60	773	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as,

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			antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension	leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectious Ceg., an infectious disease as described below under "Infectious Disease").
259 НМСFН60	773	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.

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				Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, hopercoagulation, diabetes mellitus, endocarditis, meutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, moningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectious Disease.").
260	HMDAB29	774	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the

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"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy) or
used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ohtani KI, et al., Endocrinology, 139(1):172-8 (1998); Krautheim A, et al, Exp Clin Endocrinol Diabetes, 107 (1):29-34 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from
	Insulin Secretion
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				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				cinifety. Italian I cens mat may be used	described below under injectious Disease).
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
	-			are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
		-1		immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
261	HMDAD44	775	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
			DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in adipocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			and pre-adipocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the DMEF1	neuropathy, nerve disease and nerve damage (e.g., due to
				response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				(such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
		****		promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
		-		production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
				element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
				and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
				another transcription factor that is required	stroke, and other diseases and disorders as described in the
				for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
				in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
				insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
				fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
				that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
				test for DMEF1 response element activity	diseases and disorders as described in the "Infectious
				(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
				polypeptides of the invention (including	skin), carpal tunnel syndrome and Dupuytren's
				antibodies and agonists or antagonists of	contracture). An additional highly preferred
				the invention) include assays disclosed	indication is obesity and/or complications associated with
				inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include

weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 373-L1 cells are a continuous substrain of 373 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis,
	Production of MCP-1
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	HMDAD44
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				and modulate immine cell activation	"Cardiovascular Disorders") Highly preferred indications
		**************************************		Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
			-	Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
		4		Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
		_		using techniques disclosed herein or	dysplasia.
		_		otherwise known in the art. Human	
		_		dendritic cells are antigen presenting cells	
		_		in suspension culture, which, when	
		_		activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
261	HMDAD44	775	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-

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	routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders").
	polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
	antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
-	immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
	inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
	assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
	proteins evaluate the production of	Additional highly preferred indications include
	cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
	alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
	inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
	response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
	routinely modified to test	leukemia, lymphoma, and/or as described below under
	immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
	polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
	antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
	the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
	Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
	4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
	"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
	Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
	al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
	(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
	160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
	al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
	Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
	(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
	herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
	entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
	be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
	isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
	or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
	dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
	in suspension culture, which, when	Disease").
	activated by antigen and/or cytokines,	
	initiate and upregulate T cell proliferation	
	and functional activities.	

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A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under in the control of the contr	"Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications	include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus,	endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
MIP-lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as	macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al.,	J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the
Production of MP1alpha			
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				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
263	HMEDE24	777	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			cells (such as T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
				expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
				response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
	:			publicly available (e.g., through the	allergy.

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			***	ATCC). Exemplary human I cells that	
				may be used according to these assays	
				include the SUPT cell line, which is a	
				suspension culture of IL-2 and IL-4	
				responsive T cells.	
264	HIMEDI90	778	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription of Malic	of Malic Enzyme are well-known in the art	An additional highly preferred indication is a complication
			Enzyme in adipocytes	and may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,
				invention (including antibodies and	nephropathy and/or other diseases and disorders as
				agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
				regulate transcription of Malic Enzyme, a	neuropathy, nerve disease and nerve damage (e.g., due to
				key enzyme in lipogenesis. Malic enzyme	diabetic neuropathy), blood vessel blockage, heart disease,
				is involved in lipogenesisand its expression	stroke, impotence (e.g., due to diabetic neuropathy or
				is stimulted by insulin. ME promoter	blood vessel blockage), seizures, mental confusion,
				contains two direct repeat (DR1)- like	drowsiness, nonketotic hyperglycemic-hyperosmolar
				elements MEp and MEd identified as	coma, cardiovascular disease (e.g., heart disease,
				putative PPAR response elements. ME	atherosclerosis, microvascular disease, hypertension,
				promoter may also responds to AP1 and	stroke, and other diseases and disorders as described in the
				other transcription factors. Exemplary	"Cardiovascular Disorders" section below), dyslipidemia,
				assays that may be used or routinely	endocrine disorders (as described in the "Endocrine
				modified to test for regulation of	Disorders" section below), neuropathy, vision impairment
				transcription of Malic Enzyme (in	(e.g., diabetic retinopathy and blindness), ulcers and
				adipoocytes) by polypeptides of the	impaired wound healing, and infection (e.g., infectious
				invention (including antibodies and	diseases and disorders as described in the "Infectious
				agonists or antagonists of the invention)	Diseases" section below, especially of the urinary tract and
				include assays disclosed in: Streeper, R.S.,	skin), carpal tunnel syndrome and Dupuytren's
				et al., Mol Endocrinol, 12(11):1778-91	contracture). An additional highly preferred
				(1998); Garcia-Jimenez, C., et al., Mol	indication is obesity and/or complications associated with
				Endocrinol, 8(10):1361-9 (1994); Barroso,	obesity. Additional highly preferred indications include
				I., et al., J Biol Chem, 274(25):17997-8004	weight loss or alternatively, weight gain. Aditional
				(1999); Ijpenberg, A., et al., J Biol Chem,	highly preferred indications are complications associated
				272(32):20108-20117 (1997); Berger, et	with insulin resistance.
				al., Gene 66:1-10 (1988); and, Cullen, B.,	
_				et al., Methods in Enzymol. 216:362-368	
				(1992), the contents of each of which is	
				herein incorporated by reference in its	

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		_		entirety. Hepatocytes that may be used	
_			-	according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				hepatocytes that may be used according to	
				these assays includes the H4IIE rat liver	
				hepatoma cell line.	
265 F	HMELM75	977	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
-				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
-				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
•				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
•				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,

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			entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningits, Lyme Disease, and asthma and allergy.
266	HMIAK10	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous
į			Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to

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				of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be	transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
:				used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	
592	HMIAK10	780	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
			transcription through	through the NFKB response element are well-known in the art and may be used or	inflammatory disorders. Highly preferred indications include blood disorders (e.g. as described below under
		4	element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
			cells (such as T-cells).	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
				antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
				the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
				transcription factors and modulate	described below), and immunodeficiencies (e.g., as
				expression of immunomodulatory genes.	described below). An additional highly preferred
				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
				the NFKB response element that may be	disease as described below under "Infectious Disease").
				used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"). Highly
				agonists or antagonists of the invention)	preferred indications include neoplasms and cancers, such
				include assays disclosed in Berger et al.,	as,melanoma, renal cell carcinoma, leukemia, lymphoma,
		······································		Gene 66:1-10 (1998); Cullen and Malm,	and prostate, breast, lung, colon, pancreatic, esophageal,
		****		Methods in Enzymol 216:362-368 (1992);	stomach, brain, liver and urinary cancer. Other preferred
				Henthorn et al., Proc Natl Acad Sci USA	indications include benign dysproliferative disorders and
				85:6342-6346 (1988); Black et al., Virus	pre-neoplastic conditions, such as, for example,
				Gnes 15(2):105-117 (1997); and Fraser et	hyperplasia, metaplasia, and/or dysplasia. Preferred
				al., 29(3):838-844 (1999), the contents of	indications also include anemia, pancytopenia, leukopenia,
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			====	publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
				ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
				may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
				include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs,

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				suspension culture of IL-2 and IL-4	asthma and allergy.
366	HMIAK10	780	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
	-			used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,

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according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Insulin Secretion Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion from panceatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation of insulin secretion (from pancreatic cells) by modified to test for stimulation (from pancreatic cells) by modified to test for stimulation is a factor of the invention inclined assays disclosed in: (2001); salapatek, A.M., et al., Ann. N. et al., Journal of Biondocion				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
HMIBF07 781 Insulin Secretion		-		according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
HMIBF07 781 Insulin Secretion				using techniques disclosed herein or	dysplasia.
HMIBF07 781 Insulin Secretion				otherwise known in the art. Human	
HMIBF07 781 Insulin Secretion				dendritic cells are antigen presenting cells	
HMIBF07 781 Insulin Secretion				in suspension culture, which, when	
HMIBF07 781 Insulin Secretion				activated by antigen and/or cytokines,	
HMIBF07 781 Insulin Secretion		•		initiate and upregulate T cell proliferation	
HMIBF07 781 Insulin Secretion				and functional activities.	
	HMIBF07	1	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention include assays disclosed in Shimizu, H., et al., Endocr J. 47(3):261-2(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999), Filipsson, K., et al., Ann N Y Acad Sci, 865-441-4 (1998); Olson, L.K., et al., Biol Chem, 271(28):16544-22 (1996); al Miraglia Set. al., Journal of Biomolecula Screening, 4:193-204 (1999), the conten		7		are well-known in the art and may be used	An additional highly preferred indication is a complication
of polypeptides of the invention (includin antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Shimizu, H., et al., Endocr J, 47(3):261-2(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Flipsson, K., et al., Amn NY Acad Sci, 865:441-4 (1998); Olson, L.K., et al., Journal of Bionoleculi Screening, 4:193-204 (1999), the conten				or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in disbects. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Shimizu, H., et al., Endocr 1, 47(3):261-2(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann NY Acad Sci, 865:441-4 (1998); Olson, L.K., et al., biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecule Screening, 4:193-204 (1999), the conten				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention include assays disclosed in Shimizu, H., et al., Endocr J. 47(3):261-5(2000); Salapatek, A.M., et al., Mol Endocrinol. 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecule Screening, 4:193-204 (1999), the conten				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J. 47(3):261-5(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); a Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann NY Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); a Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-5(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); a Miraglia S et. al., Journal of Biomolecula Screening, 4:193-204 (1999), the contennance of t				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-5 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-5(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); altiraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Shimizu, H., et al., Endocr J. 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann NY Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann NY Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten		-		key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-5 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-5 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed it Shimizu, H., et al., Endocr J, 47(3):261-5 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecul Screening, 4:193-204 (1999), the conten				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
antibodies and agonists or antagonists of the invention) include assays disclosed ir Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecul Screening, 4:193-204 (1999), the contem				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
the invention) include assays disclosed in Shimizu, H., et al., Endocr J, 47(3):261-5 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
(2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomoleculi Screening, 4:193-204 (1999), the conten				Shimizu, H., et al., Endocr J, 47(3):261-9	diseases and disorders as described in the "Infectious
Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecul Screening, 4:193-204 (1999), the conten				(2000); Salapatek, A.M., et al., Mol	Diseases" section below, especially of the urinary tract and
Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecul Screening, 4:193-204 (1999), the contem				Endocrinol, 13(8):1305-17 (1999);	skin), carpal tunnel syndrome and Dupuytren's
865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecul Screening, 4:193-204 (1999), the conten				Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
Biol Chem, 271(28):16544-52 (1996); an Miraglia S et. al., Journal of Biomolecul: Screening, 4:193-204 (1999), the conten				865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
Miraglia S et. al., Journal of Biomolecul Screening, 4:193-204 (1999), the conten				Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
Screening, 4:193-204 (1999), the conten				Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
				Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
of each of which is herein incorporated b				of each of which is herein incorporated by	with insulin resistance.

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A highly preferred indication is diabetes mellitus. Secretion from are well-known in the art and may be used pancreatic beta cells. or routinely modified to assess the ability pancreatic beta cells. or routinely modified to assess the ability pancreatic beta cells. or routinely modified to assess the ability pancreatic beta cells. or routinely modified to assess the ability pancreatic beta cells. or routinely modified to assess the ability antibodies and agonists or antagonists of is measured by FMAT using anti-rat pancreatic beta cells is upregulated by pancreatic beta cells is upregulated by pancreatic beta cells is upregulated by pancreatic beta cells is upregulation is a key component in diabetes. Exemplary proteins/peptides, and disregulation of insulin secretion (from pancreatic cells) by Disorders' section below), diabetic neuropathy, incred giasease and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and disorders as troke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease, hypertension, sasays that may be used and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention of insulin is exertion (from pancreatic cells) by plyopetides of the invention (including the company of the invention (including) the company of the invention (including the company of the invention (including) the company of the invention (including the company of the invention (including the company of the i
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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's 7-9 contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. S-1 sl an al.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for inhibiting led or inhibiting led o
Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including
	Endothelial Cell Apoptosis
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	antibodies and agonists or antagonists of the invention) include the assays disclosed	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for
	in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
-	(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
	218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
	Atheroscler Thromb 3(2): 75-80 (1996);	.♀
	the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
	incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
	Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
	according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
	available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
	sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
	may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
	include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
	(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
	endothelial cells which line blood vessels	overload, and/or as described below under
	and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
	but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
	vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
	immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
-		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous), glomus tumors, telangiectasia,
		bacillary angiomatosis, hemangioendothelioma,
		angiosarcoma, haemangiopericytoma, lymphangioma,
		lymphangiosarcoma. Highly preferred indications also
		include cancers such as, prostate, breast, lung, colon,
		pancreatic, esophageal, stomach, brain, liver, and urinary
		cancer. Preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,

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example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Tamune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and atssues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and	
polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis,
as T-cells).	Upregulation of HLA- DR and activation of T cells
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lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and alternatively, suppressing a T cell-mediated immune response. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and	disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section	below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly	weight gain. Aditional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. An additional preferred indication is infection (e.g., AIDS, and/or as described below under "Infectious Disease").
systemic lupus erythematosis, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II expressing T cells and antigen presenting cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate	the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of MHC class II products, such as HLA-DR antigens, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polymentides of the invention (including	antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Lamour et al., Clin Exp Immunol 89(2):217-222 (1992); Hurme and Sihvola, Immunol Lett 20(3):217-222 (1989); Gansbacher and Zier, Cell Immunol	Histochem Cytochem 40(11):1675-1683, the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are
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				primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and
270	HMJAK70	784	Proliferation, and/or cytokine production in immune cells (such as T-cells).	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation., and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345	Inflammatory disorders, and astima and ailergy. Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.

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			(2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the	
271 HMSBE04	785	Activation of transcription through API response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic
			incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,

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meningitis, and Lyme Disease.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma
may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1997); Aramburau et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995), and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh
	Activation of transcription through NFKB response element in immune cells (such as B-cells).
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	HMSCL38
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		ريس بسعدار وحد		B-cell line.	
273	HMSCR69	787	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
			-	monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	~
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
			+ *************************************	Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
		,		immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	

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				dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation and functional activities.	
274	HMSHC86	788	Activation of Skeletal	Kinase assay. Kinase assays, for examplek	Highly preferred indications include endocrine
			Muscle Cell ERK	Elk-1 kinase assays, for ERK signal	disorders (e.g., as described below under "Endocrine
			Signalling Pathway	transduction that regulate cell proliferation	Disorders') and disorders of the musculoskeletal system.
				or differentiation are well known in the art	Preferred indications include neoplastic diseases (e.g., as
				and may be used or routinely modified to	described below under "Hyperproliterative Disorders"),
				assess the ability of polypeptides of the	blood disorders (e.g., as described below under "Immune
				invention (including antibodies and	Activity', "Cardiovascular Disorders", and/or "Blood-
				agonists or antagonists of the invention) to	Related Disorders"), immune disorders (e.g., as described
				promote or inhibit cell proliferation,	below under "Immune Activity"), neural disorders (e.g., as
				activation, and differentiation. Exemplary	described below under "Neural Activity and Neurological
				assays for ERK kinase activity that may be	on (e
				used or routinely modified to test ERK	"Infectious Disease"). A highly preferred indication
	•			kinase-induced activity of polypeptides of	is diabetes mellitus. An additional highly preferred
				the invention (including antibodies and	indication is a complication associated with diabetes (e.g.,
				agonists or antagonists of the invention)	diabetic retinopathy, diabetic nephropathy, kidney disease
				include the assays disclosed in Forrer et	(e.g., renal failure, nephropathy and/or other diseases and
				al., Biol Chem 379(8-9):1101-1110	disorders as described in the "Renal Disorders" section
				(1998); Le Marchand-Brustel Y, Exp Clin	below), diabetic neuropathy, nerve disease and nerve
				Endocrinol Diabetes 107(2):126-132	damage (e.g., due to diabetic neuropathy), blood vessel
				(1999); Kyriakis JM, Biochem Soc Symp	blockage, heart disease, stroke, impotence (e.g., due to
				64:29-48 (1999); Chang and Karin, Nature	diabetic neuropathy or blood vessel blockage), seizures,
				410(6824):37-40 (2001); and Cobb MH,	mental confusion, drowsiness, nonketotic hyperglycemic-
				Prog Biophys Mol Biol 71(3-4):479-500	hyperosmolar coma, cardiovascular disease (e.g., heart
				(1999); the contents of each of which are	disease, atherosclerosis, microvascular disease,
		•		herein incorporated by reference in its	hypertension, stroke, and other diseases and disorders as
				entirety. Rat myoblast cells that may be	described in the "Cardiovascular Disorders" section
				used according to these assays are publicly	below), dyslipidemia, endocrine disorders (as described in
				available (e.g., through the ATCC).	the "Endocrine Disorders" section below), neuropathy,
				Exemplary rat myoblast cells that may be	vision impairment (e.g., diabetic retinopathy and
				used according to these assays include L6	blindness), ulcers and impaired wound healing, infection
				cells. L6 is an adherent rat myoblast cell	(e.g., infectious diseases and disorders as described in the
				line, isolated from primary cultures of rat	"Infectious Diseases" section below, especially of the

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			thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Highly preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
275	HMSHU20	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T immunodeficiency (e.g., as described below), boosting a T

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	_		of (noting or antegonistic of the inventor) to	Lea T conjugation and contracting a T cell.
			agoinsts of antagoinsts of the invention) to	
			mediate immunomodulation, regulate	mediated immune response. Additional nigniy preterred
			inflammatory activities, modulate TH2	indications include inflammation and inflammatory
	****		helper cell function, and/or mediate	disorders. Additional preferred indications include
			humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
			Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
			immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
			production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
			gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
			cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
			routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
			immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
			polypeptides of the invention (including	include benign dysproliferative disorders and pre-
			antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
			the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
			in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
			Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
			Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
•			Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
			(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
			15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
			(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
-			of each of which are herein incorporated	
		-	by reference in its entirety. Human T cells	
			that may be used according to these assays	
			may be isolated using techniques disclosed	
			herein or otherwise known in the art.	
			Human T cells are primary human	
			lymphocytes that mature in the thymus and	
			express a T Cell receptor and CD3, CD4,	
			or CD8. These cells mediate humoral or	
			cell-mediated immunity and may be	
			preactivated to enhance responsiveness to	
\dashv	1		immunomodulatory factors.	
276 HMSHY25	5 790	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed	A highly preferred embodiment of the invention

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by activated T cells, macrophages,	includes a method for stimulating the production of GM-
endothelial cells, and fibroblasts. GM-	CSF. An alternative highly preferred embodiment of the
 CSF regulates differentiation and	invention includes a method for inhibiting the production
 proliferation of granulocytes- macrophage	of GM-CSF. Highly preferred indications include
progenitors and enhances antimicrobial	inflammation and inflammatory disorders. An additional
activity in neutrophils, monocytes and	Ö
macrophage. Additionally, GM-CSF plays	below under "Infectious Disease". Highly preferred
an important role in the differentiation of	indications include blood disorders (e.g., neutropenia (and
dendritic cells and monocytes, and	the prevention of neutropenia (e.g., in HIV infected
increases antigen presentation. GM-CSF	patients), and/or as described below under "Immune
is considered to be a proinflammatory	Activity", "Blood-Related Disorders", and/or
cytokine. Assays for immunomodulatory	"Cardiovascular Disorders"). Highly preferred indications
proteins that promote the production of	also include autoimmune diseases (e.g., rheumatoid
GM-CSF are well known in the art and	arthritis, systemic lupus erythematosis, multiple sclerosis
may be used or routinely modified to	and/or as described below) and immunodeficiencies (e.g.,
assess the ability of polypeptides of the	as described below). Additional highly preferred
invention (including antibodies and	indications include asthma. Highly preferred indications
agonists or antagonists of the invention) to	include neoplastic diseases (e.g., leukemia (e.g., acute
mediate immunomodulation and modulate	lymphoblastic leukemia, and acute myelogenous
the growth and differentiation of	leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and
leukocytes. Exemplary assays that test for	Hodgkin's disease), and/or as described below under
immunomodulatory proteins evaluate the	"Hyperproliferative Disorders"). Highly preferred
production of cytokines, such as GM-CSF,	indications include neoplasms and cancers, such as,
and the activation of T cells. Such assays	leukemia, lymphoma, melanoma, and prostate, breast,
that may be used or routinely modified to	lung, colon, pancreatic, esophageal, stomach, brain, liver
test immunomodulatory activity of	and urinary cancer. Other preferred indications include
polypeptides of the invention (including	benign dysproliferative disorders and pre-neoplastic
antibodies and agonists or antagonists of	conditions, such as, for example, hyperplasia, metaplasia,
the invention) include the assays disclosed	and/or dysplasia. Highly preferred indications include:
in Miraglia et al., J Biomolecular	suppression of immune reactions to transplanted organs
 Screening 4:193-204 (1999); Rowland et	and tissues (e.g., bone marrow transplant); accelerating
 al., "Lymphocytes: a practical approach"	myeloid recovery; and mobilizing hematopoietic
 Chapter 6:138-160 (2000); and Ye et al., J	progenitor cells. Preferred indications include boosting
Leukoc Biol (58(2):225-233, the contents	a T cell-mediated immune response, and alternatively,
of each of which are herein incorporated	suppressing a T cell-mediated immune response.
by reference in its entirety. Natural killer	Preferred indications include anemia, pancytopenia,
cells that may be used according to these	leukopenia, thrombocytopenia, acute lymphocytic anemia

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				assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	(ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.
276	HMSHY25	790	Production of IFNgamma using Natural Killer cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes IgG2a and inhibits IgE; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" (e.g. cancer/tumorigenesis) and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing antibody-dependent immune responses, boosting innate immunity and immune responses, and suppressing innate immunity and immune responses. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include idiopathic pulmonary fibrosis. Highly preferred indications include idiopathic pulmonary and/or service (e.g., leukemia, lymphoma, melanoma, and/or as

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			antibodies and agonists or antagonists of	Highly preferred indications include neoplasms and
			the invention) include the assays disclosed	cancers, such as, for example, leukemia, lymphoma,
			In Miraglia et al., J Biomolecular	melanoma, and prostate, breast, lung, colon, pancreatic,
			Screening 4:193-204 (1999); Kowiana et	Other angles of indication in the fand uninary cancer.
			al., Lymphocytes: a practical approach	disorders and man assemble to the series and the form
			Cliapter 0:136-100 (2000);	disorders and pre-neopiastic conditions, such as, for example hyperplacia metaplacia and/or dyenlacia
			Billian et al., Ann NY Acad Sci 856:22-32	Preferred indications include anemia, pancytopenia.
-			(1998); Boehm et al., Annu Rev Immunol	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			15:749-795 (1997), and Rheumatology	lymphocytic anemia (ALL), plasmacytomas, multiple
•			(Oxford) 38(3):214-20 (1999), the contents	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			of each of which are herein incorporated	granulomatous disease, inflammatory bowel disease,
			by reference in its entirety. Natural Killer	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			(NK) cells that may be used according to	immune reactions to transplanted organs and tissues,
			these assays are publicly available (e.g.,	hemophilia, hypercoagulation, diabetes mellitus,
			through the ATCC) or may be isolated	endocarditis, meningitis, Lyme Disease, asthma and
** .*			using techniques disclosed herein or	allergy.
			otherwise known in the art. Natural killer	
			(NK) cells are large granular lymphocytes	
			that have cytotoxic activity but do bind	
			antigen. NK cells show antibody-	
			independent killing of tumor cells and also	
			recognize antibody bound on target cells,	
			via NK Fc receptors, leading to cell-	
			mediated cytotoxicity.	
277 HMTAB77	791	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
			growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
			transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated

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				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
		_		agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
		_		Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
07.0	THATTARDA	702	10 Jake 11:1 A:11	3	under "Infectious Disease").
0/7	TIMIO ACTO	761	Endounciiai Ceii	Caspase Apoptosis. Assays for caspase	A nigniy preience embournent of the invention
			Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
				may be used or routinely modified to	An alternative highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includés a method for inhibiting endothelial cell
				invention (including antibodies and	growth. A highly preferred embodiment of the
				agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
				promote caspase protease-mediated	cell proliferation. An alternative highly preferred
					metho
				endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly

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	of tumors is	of tumors is associated with tumor	preferred embodiment of the invention includes a method
	regression du	regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
	supply. Ex	supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
	apoptosis that	apoptosis that may be used or routinely	includes a method for inhibiting (e.g., decreasing)
-	modified to t	modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
	of polypeptic	of polypeptides of the invention (including	embodiment of the invention includes a method for
	antibodies ar	antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
	the invention	the invention) include the assays disclosed	embodiment of the invention includes a method for
	in Lee et al.,	in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
	(2000); Nor	(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
	218 (2000);	218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
	Atheroscler	Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
	the contents	the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
	incorporated	incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
	Endothelial	Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
	according to	according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
	available (e.	available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
	sources). Ex	sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
	may be used	may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
	include bovi	include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
	(bAEC), whi	(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
	endothelial c	endothelial cells which line blood vessels	overload, and/or as described below under
	and are invo	and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
	but are not li	but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
	vascular per	vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
	immune cell	immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
			themselves, such as of the arteries, capillaries, veins and/or
			lymphatics). Highly preferred are indications that
			stimulate angiogenesis and/or cardiovascularization.
			Highly preferred are indications that inhibit angiogenesis
			and/or cardiovascularization. Highly preferred
			indications include antiangiogenic activity to treat solid
			tumors, leukemias, and Kaposi's sarcoma, and retinal
			disorders. Highly preferred indications include neoplasms
			and cancer, such as, Kaposi's sarcoma, hemangioma
			(capillary and cavernous), glomus tumors, telangiectasia,
			bacillary angiomatosis, hemangioendothelioma,

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					inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
278	HMUAE26	792		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	inch
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
				invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
				agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
			4-1-2-44-	mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
				inflammatory activities, modulate TH2	indications include inflammation and inflammatory
				helper cell function, and/or mediate	disorders. Additional preferred indications include
			,	humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
				Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
				immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
				production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
				gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
				immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
				polypeptides of the invention (including	include benign dysproliferative disorders and pre-
				antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
				the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
				in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
				Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
				Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				J Clin Lab Anal 8(3):223-233 (1993);	disease, inflammatory bowel disease, sepsis, neutropenia,

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neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and
Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human I ymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al.,
	Stimulation of insulin secretion from pancreatic beta cells.
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w. in G S King We by in G S King W.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune
antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
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response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the
assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is a suspension culture of IL-2 dependent T cells that also respond to IL-4.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or
	Regulation of apoptosis in pancreatic beta cells.
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"Can ended bise ended bise ended bise ended bise bise skin cont india obes weight high high high high high high high	creted by includes a method for inhibiting (e.g., reducing) IL-5 s, and production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g.,
antagonists of the invention) include the assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Brandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett, 455(3):315-30 (1999); Lee et al., FEBS Lett, 455(3):315-30 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1980 77:3519.	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil
	Production of IL-5
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	function and B cell Ig production and	increasing) IL-5 production. A highly preferred
	promote polarization of CD4+ cells into	embodiment of the invention includes a method for
	TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
	may be used or routinely modified to	An alternative highly preferred embodiment of the
	assess the ability of polypeptides of the	invention includes a method for inhibiting (e.g.,
	invention (including antibodies and	decreasing) immunoglobulin production. A highly
	agonists or antagonists of the invention) to	
	mediate immunomodulation, stimulate	
	immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
-	production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
	polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
	cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
	assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
	proteins evaluate the production of	described below under "Immune Activity", "Blood-
	cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
	stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
	cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
	be used or routinely modified to test	multiple sclerosis and/or as described below) and
	immunomodulatory activity of	immunodeficiencies (e.g., as described below).
	polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
	antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
	the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
	in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
	Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
	al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
	Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
	Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
	Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
	Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
	Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
	Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
	contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
	incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
	Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
	to these assays may be isolated using	immune reactions to transplanted organs and tissues,
	techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
	Known in the art. Human I cells are	endocarditis, meningitis, and Lyme Disease.

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				primary human lymphocytes that mature in the thymus and express a T cell receptor	
				and CD3, CD4, or CD8. These cells	
				mediate humoral or cell-mediated	
				immunity and may be preactivated to	
,				enhance responsiveness to	٠
				immunomodulatory factors.	
284	HNEAK81	862	Production of	MIP-laipha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
			•	activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or routinely modified to	(e.g., an infectious disease as described below under
•				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
				agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
				mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
				chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
				differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
				for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
				the production of chemokines, such as	described below). Additional highly preferred indications
				macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
				monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
				modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary

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HNECL22 75	799	Activation of transcription through NFKB response element in immune cells (such as T-cells).	2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, and/or dysplasia. Preferred indications include benign dysproliferative disorders and hyperplasia, and prostate and prostate and prostate and prostate and animary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, and/or dysplasia.
			each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous

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				publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, sumression of immine reactions to transplanted organs
				suspension culture of IL-2 and IL-4 responsive T cells.	suppression of minimum reactions to transplanted of gains, asthma and allergy.
286	HNECW49	008	Proliferation,	Kinase assays, for example kinase assays	Preferred embodiments of the invention include using
			cytokine production in	ior members of the MAP kinase family (including p38, JAK, and ERK) are well	polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention.
			immune cells (such as	known in the art and may be used or	and/or treatment of inflammation, infection, allergy,
			T-cells).	routinely modified to assess the ability of	asthma, autoimmunity, and cancer.
				polypeptides of the invention (including	
				antibodies and agonists or antagonists of	
				the invention) to promote or inhibit cell	
				proliferation, differentiation., and/or	
				cytokine production in immune cells such	
				as T-cells. Exemplary assays for MAP	
	-			kinase family members that may be used	
				or routinely modified to test polypeptides	
				of the invention (including antibodies and	
				agonists or antagonists of the invention)	
				include the assays disclosed in: Rincon M.,	
				Curr Opin Immunol; 13(3):339-345	
				(2001); Wang LH, et al., J Immunol,	
				162(7):3897-3904 (1999); Sakamoto H, et	
				al., J Biol Chem, 275(46):35857-35862	
				(2000), the contents of each of which are	
				herein incorporated by reference in its	
				entirety. Exemplary immune cells (for	
				example, T-cells) that may be used	
				according to these assays include the	
				mouse CTLL cell line.	
287	HNEDH88	801	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as 1-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious

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				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
288	HNFAC50	805	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	Preferred embodiments of the invention include using
			of immune cells (such	apoptosis are well known in the art and	polypeptides of the invention (or antibodies, agonists, or
			as mast cells).	may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
				assess the ability of polypeptides of the	and/or treatment of asthma, allergy, hypersensitivity and
				invention (including antibodies and	inflammation.
				agonists or antagonists of the invention) to	
				regulate caspase protease-mediated	
				apoptosis in immune cells (such as, for	
				example, in mast cells). Mast cells are	
				found in connective and mucosal tissues	

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy) or
throughout the body, and their activation via immunoglobulin E -antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent
	Regulation of viability and proliferation of pancreatic beta cells.
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				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
	.,			invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
				(1998), the contents of each of which is	obesity. Additional highly preferred indications include
		-		herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
		- 3		beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
290	HNFHF34	804	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or routinely modified to	(e.g., an infectious disease as described below under

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			assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
			invention (including antibodies and	blood disorders (e.g., as described below under "Immune
			agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
			mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
			chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
			differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
			for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
			the production of chemokines, such as	described below). Additional highly preferred indications
			macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				Preferred indications also include anemia, pancytopenia,
			monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
			modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
			invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
			include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
			J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
	****		204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
			a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
			(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
			Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
			al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
			Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
			2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
	-		Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
			each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
			reference in its entirety. Human dendritic	dysplasia.
	·= ··		cells that may be used according to these	
			assays may be isolated using techniques	
			disclosed herein or otherwise known in the	
			art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
			proliferation and functional activities.	
291 HNGAK51	1 805	Insulin Secretion	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.

described in the "Renal Disorders" section below), diabetic An additional highly preferred indication is a complication stroke, and other diseases and disorders as described in the Diseases" section below, especially of the urinary tract and diabetic neuropathy), blood vessel blockage, heart disease, Disorders" section below), neuropathy, vision impairment Aditional neuropathy, nerve disease and nerve damage (e.g., due to "Cardiovascular Disorders" section below), dyslipidemia, indication is obesity and/or complications associated with highly preferred indications are complications associated diabetic nephropathy, kidney disease (e.g., renal failure, obesity. Additional highly preferred indications include impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious stroke, impotence (e.g., due to diabetic neuropathy or atherosclerosis, microvascular disease, hypertension, drowsiness, nonketotic hyperglycemic-hyperosmolar (e.g., diabetic retinopathy and blindness), ulcers and endocrine disorders (as described in the "Endocrine blood vessel blockage), seizures, mental confusion, nephropathy and/or other diseases and disorders as associated with diabetes (e.g., diabetic retinopathy, coma, cardiovascular disease (e.g., heart disease, An additional highly preferred skin), carpal tunnel syndrome and Dupuytren's weight loss or alternatively, weight gain. with insulin resistance. contracture). of polypeptides of the invention (including Biol Chem, 271(28):16544-52 (1996); and, are well-known in the art and may be used that may be used according to these assays Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents ATCC) and/or may be routinely generated of each of which is herein incorporated by epithelial cell line established from Syrian the invention) include assays disclosed in: hamster islet cells transformed with SV40. or routinely modified to assess the ability insulin antibodies. Insulin secretion from Shimizu, H., et al., Endocr J, 47(3):261-9 secretion. For example, insulin secretion modified to test for stimulation of insulin antibodies and agonists or antagonists of antibodies and agonists or antagonists of reference in its entirety. Pancreatic cells polypeptides of the invention (including proteins/peptides, and disregulation is a HITT15 Cells. HITT15 are an adherent key component in diabetes. Exemplary Filipsson, K., et al., Ann N Y Acad Sci, are publicly available (e.g., through the Exemplary pancreatic cells that may be 865:441-4 (1998); Olson, L.K., et al., J pancreatic beta cells is upregulated by used according to these assays include is measured by FMAT using anti-rat assays that may be used or routinely (2000); Salapatek, A.M., et al., Mol secretion (from pancreatic cells) by Endocrinol, 13(8):1305-17 (1999); the invention) to stimulate insulin These cells express glucagon, glucose and also by certain

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				somatostatin, and glucocorticoid receptors.	
				The cells secrete insulin, which is	
				stimulated by glucose and glucagon and	
				suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
292	HNGAM58	908	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,

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				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis I yang Disease cardiac reperfusion injury and
					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
292	HNGAM58	908	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells.	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				home and has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired immunoresponses. Assays for	proliteration. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell
	<u>.</u> .			immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				CD8+ T cells are well known in the art and	Activity, blood-related Disolders, and of a "Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agomists of antagomists of the invention) to modulate the activation of T cells,	below), ocosting a 1 cen-mediated infinitive response, and suppressing a T cell-mediated immune response.
-				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for

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example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, inflammation and inflammatory disorders, and asthma and allergy. An additional preferred indication is infection (e.g., as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include inflammation and inflammatory
(including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
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assays disclosed in Berger et al., Gene 66:1-10 (1998): Cullen and Malm.	disorders. Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. An
(1997); Parra et al., J Immunol	additional highly preferred indication includes infection
166(4):2437-2443 (2001); and Butscher et	(e.g., AIDS, and/or as described below under "Infectious
al., J Biol Chem 3(1):552-560 (1998), the	Disease"). Highly preferred indications include
contents of each of which are herein	neoplastic diseases (e.g., melanoma, renal cell carcinoma,
incorporated by reference in its entirety. T	leukemia, lymphoma, and/or as described below under
cells that may be used according to these	"Hyperproliferative Disorders"). Highly preferred
assays are publicly available (e.g., through	indications include neoplasms and cancers, such as, for
the ATCC). Exemplary human T cells that	example, melanoma (e.g., metastatic melanoma), renal cell
may be used according to these assays	carcinoma (e.g., metastatic renal cell carcinoma),
include the JURKAT cell line, which is a	leukemia, lymphoma (e.g., T cell lymphoma), and
suspension culture of leukemia cells that	prostate, breast, lung, colon, pancreatic, esophageal,
produce IL-2 when stimulated.	stomach, brain, liver and urinary cancer. Other preferred
	indications include benign dysproliferative disorders and
	pre-neoplastic conditions, such as, for example,
	hyperplasia, metaplasia, and/or dysplasia. A highly
	preferred indication is infection (e.g., tuberculosis,
	infections associated with granulomatous disease, and
	osteoporosis, and/or an infectious disease as described
	below under "Infectious Disease"). A highly preferred
	indication is AIDS. Additional highly preferred
	indications include suppression of immune reactions to
	transplanted organs and/or tissues, uveitis, psoriasis, and
	tropical spastic paraparesis. Preferred indications
	include blood disorders (e.g., as described below under
	"Immune Activity", "Blood-Related Disorders", and/or
	"Cardiovascular Disorders"). Preferred indications also
	include anemia, pancytopenia, leukopenia,
	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	anemia (ALL), plasmacytomas, multiple myeloma,
	Burkitt's lymphoma, arthritis, granulomatous disease,
	inflammatory bowel disease, sepsis, neutropenia,

					neutrophilia, hemophilia, hypercoagulation, diabetes
					mellitus, endocarditis, meningitis, Lyme Disease, asthma
294	HNGDQ38	808	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
	,			imminomodulatory proteins that are	includes a method for ctimulating (e.g. increasing) MCD 1
				minimum density proteins that are	includes a include tot stimulating (e.g., incleasing) incl. =1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
	•			Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
	•			production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
		· · · · · ·		and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
		,		contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
	····			incorporated by reference in its entirety.	cancer. Other preferred indications include benign
	_			Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or